

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Mike Mellow Examiner #: 69404 Date: 2/13/03
Art Unit: 1654 Phone Number 30 8-4230 Serial Number: 0101026, 408
Mail Box and Bldg/Room Location: CM1 10A03 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MEJ

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Cytostatic - integrin conjugates having specifically...
Inventors (please provide full names): Lerchen Hans-Georg; Baumgarten Jörg;
Lockhoff ~~Wolfgang~~; Albers Markus; Schoop Andreas
Earliest Priority Filing Date: 12/27/2000

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please Search Example 2
on all relevant databases.
i.e. CAS, Biosis, Medline, Registry,
etc.

Point of Contact:
Beverly Shears
Technical Info. Specialist
CM1 1E05 Tel: 308-4994

STAFF USE ONLY		Type of Search	Vendors and cost where applicable
Searcher: Beverly 24994	NA Sequence (#)	STN	✓
Searcher Phone #:	AA Sequence (#)	Dialog	
Searcher Location:	Structure (#)	Questel/Orbit	
Date Searcher Picked Up:	Bibliographic	Dr. Link	
Date Completed: 02-14-03	Litigation	Lexis/Nexis	
Searcher Prep & Review Time: 12	Fulltext	Sequence Systems	
Clerical Prep Time:	Patent Family	WWW/Internet	
Online Time: 10	Other	Other (specify)	

10/026408

283613-52-5P 283613-53-6P 283613-54-7P 283613-55-8P
283613-56-9P 283613-57-0P 283613-58-1P 283613-59-2P
283613-60-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. of .beta.-phenylalanine derivs. as integrin antagonists)

L8 ANSWER 4 OF 5 MARPAT COPYRIGHT 2003 ACS

(ALL HITS ARE ITERATION INCOMPLETES)

ACCESSION NUMBER: 133:89443 MARPAT

TITLE: Quinolonecarboxamides as antiviral agents,
especially against viruses of the herpes family

INVENTOR(S): Turner, Steven Ronald; Strohbach, Joseph Walter;
Thaisrivongs, Suvit; Vaillancourt, Valerie A.;
Schnute, Mark E.; Tucker, John Alan

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

SOURCE: PCT Int. Appl., 219 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

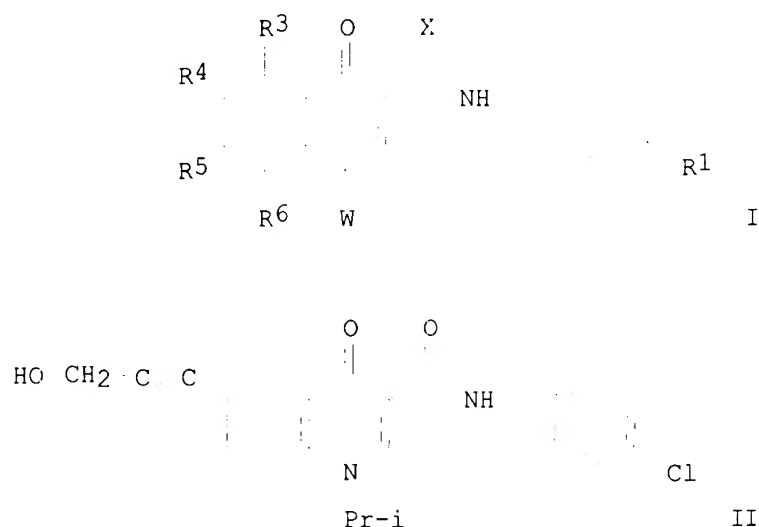
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000040561	A1	20000713	WO 1999-US27960	19991222
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6248739	B1	20010619	US 1999-466712	19991217
EP 1140850	A1	20011010	EP 1999-967145	19991222
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002534416	T2	20021015	JP 2000-592270	19991222
NO 2001003383	A	20010907	NO 2001-3383	20010706
PRIORITY APPLN. INFO.:			US 1999-115301P	19990108
			US 1999-140610P	19990623
			WO 1999-US27960	19991222

GI



- AB The invention provides quinolinecarboxamides I (X = O, S; W = R₂, etc., where R₁-R₆ = a wide variety of defined groups, with 125 examples), e.g., hydroxypropynyl deriv. II, and their pharmaceutically acceptable salts which are useful as antiviral agents, in particular, as agents against viruses of the herpes family. Activities of the compds. against HCMV, HSV, and VZV polymerase are presented. Pharmaceutical compns. comprising compds. I are claimed (no examples).
- IC ICM C07D215-16
ICS C07D215-18; C07D215-22; C07D215-36; C07D215-38; C07D215-58; C07D215-233; A61K031-47; A61P031-12
- CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
- ST quinolinecarboxamide prepn antiviral agent; herpes virus
quinolinecarboxamide antiviral agent
- IT Antiviral agents
(quinolinecarboxamides as antiviral agents)
- IT Human herpesvirus 4
(quinolinecarboxamides for treatment of Epstein-Barr virus)
- IT Cytomegalovirus
(quinolinecarboxamides for treatment of cytomegalovirus)
- IT Human herpesvirus 1
(quinolinecarboxamides for treatment of herpes simplex virus type 1)
- IT Human herpesvirus 2
(quinolinecarboxamides for treatment of herpes simplex virus type 2)
- IT Human herpesvirus 6
(quinolinecarboxamides for treatment of human herpes virus type 6)
- IT Human herpesvirus 7
(quinolinecarboxamides for treatment of human herpes virus type 7)
- IT Human herpesvirus
(quinolinecarboxamides for treatment of human herpes viruses)
- IT Human herpesvirus 3

- (quinolinecarboxamides for treatment of varicella zoster virus)
- IT Amides, preparation
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (quinolinecarboxamides; prepn. of quinolinecarboxamides as antiviral agents)
- IT 29943-42-8, Tetrahydro-4H-pyran-4-one
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (conversion to oxazepanone and for prepn. of quinolinecarboxamide derivs.)
- IT 1072-72-6, Tetrahydrothiopyran-4-one
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (conversion to thiazepane)
- IT 7771-02-9, 3-Bromo-4-fluorobenzaldehyde
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (for benzylation of morpholine)
- IT 57-14-7, 1,1-Dimethylhydrazine 75-26-3, 2-Bromopropane 87-13-8, Diethyl ethoxymethylenemalonate 100-11-8, 4-Nitrobenzyl bromide 102-71-6, reactions 104-63-2, N-Benzylethanolamine 104-86-9, 4-Chlorobenzylamine 106-93-4, 1,2-Dibromoethane 107-08-4, 1-Iodopropane 107-19-7, Propargyl alcohol 110-65-6, 1,4-Butynediol 110-73-6 110-77-0, Ethyl 2-hydroxyethyl sulfide 110-91-8, Morpholine, reactions 111-46-6, reactions 111-90-0, 2-Ethoxy-(2-ethoxy)ethanol 112-35-6, Triethyleneglycol monomethyl ether 140-75-0, 4-Fluorobenzylamine 350-46-9, 1-Fluoro-4-nitrobenzene 352-34-1, 4-Fluoriodobenzene 505-10-2, 3-Methylthiopropanol 513-48-4, 2-Iodobutane 540-37-4, 4-Iodoaniline 615-43-0, 2-Iodoaniline 622-08-2, 2-Benzyloxyethanol 628-89-7, 2-(2-Chloroethoxy)ethanol 699-12-7, 2-Hydroxyethyl phenyl sulfide 881-95-8, dl-Metanephine hydrochloride 927-74-2, 3-Butyn-1-ol 1069-72-3 1445-73-4, N-Methyl-4-piperidone 1479-24-9, Ethyl 3-(2-fluorophenyl)-3-oxopropanoate 2008-75-5, 1-(2-Chloroethyl)piperidine hydrochloride 2213-43-6, 1-Aminopiperidine 2373-51-5, Chloromethyl methyl sulfide 3647-69-6, N-(2-Chloroethyl)morpholine hydrochloride 3970-21-6, 2-Methoxyethoxymethyl chloride 4261-68-1, 2-(Diisopropylamino)ethyl chloride hydrochloride 4319-49-7, 4-Aminomorpholine 4584-46-7, Dimethylaminoethyl chloride hydrochloride 5188-07-8, Sodium thiomethoxide 5292-43-3, tert-Butyl bromoacetate 5407-04-5, 3-Dimethylaminopropyl chloride hydrochloride 5466-88-6, (2H)1,4-Benzoxazin-3(4H)-one 5472-49-1, N-(3-Chloropropyl)piperidine hydrochloride 6148-64-7, Potassium ethyl malonate 6542-54-7 6589-55-5, .alpha.-(Methylaminomethyl)benzyl alcohol 6928-85-4, 1-Amino-4-methylpiperazine 6972-79-8, 1,3-Dibenzoyloxy-2-propanol 7205-90-5, Chloromethyl 4-chlorophenyl sulfide 7205-91-6, Chloromethyl phenyl sulfide 7250-67-1, 1-(2-Chloroethyl)pyrrolidine hydrochloride 10595-09-2, 3,3'-Thiodipropanol 16589-24-5, Synephrine 16596-41-1, 1-Aminopyrrolidine 17201-43-3, 4-(Bromomethyl)benzonitrile 18621-18-6, 3-Azetidinol hydrochloride 21151-56-4, .alpha.,4-Dichloroanisole 26177-44-6, 4-Bromobenzylamine hydrochloride 27374-25-0, [(1-Ethoxycyclopropyl)oxy]trimethylsilane 29632-74-4, 2-Fluoro-4-iodoaniline 31560-06-2 33821-94-2, 2-(3-Bromopropoxy)tetrahydro-2H-pyran 50586-80-6, 2-(2-Methoxyethoxy)ethyl p-toluenesulfonate 54288-69-6, 2-Chloromethyl-1-methylpyrrolidine hydrochloride 58305-05-8 72748-99-3, (R)-1-Amino-2-(methoxymethyl)pyrrolidine 79099-07-3,

- 1-(tert-Butoxycarbonyl)-4-piperidone 84466-87-5,
 4-(Azidomethyl)benzonitrile 117924-33-1 121838-84-4
 132091-42-0 281652-58-2, 2-Chloro-5-iodobenzoyl chloride
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (for prepn. of quinolinecarboxamide derivs.)
- IT 2767-70-6P, 4-Nitrobenzyltriphenylphosphonium bromide 5638-60-8P
 6425-46-3P, 4-(4-Nitrobenzyl)morpholine 10406-25-4P,
 4-(Aminomethyl)benzonitrile 21987-29-1P, 4,4-Difluoropiperidine
 51013-67-3P, 4-(4-Aminobenzyl)morpholine 101184-85-4P
 124700-41-0P, 2-Fluoro-5-iodobenzoic acid 281651-96-5P,
 N-Cyclopropyl-4-iodoaniline 281652-00-4P 281652-01-5P
 281652-05-9P 281652-10-6P, tert-Butyl 4,4-difluoro-1-
 piperidinecarboxylate 281652-11-7P, 4-Fluoro-1,2,3,6-
 tetrahydropyridine hydrochloride 281652-25-3P,
 4-(3-Bromo-4-fluorobenzyl)morpholine 281652-26-4P 281652-27-5P
 281652-40-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)
 (for prepn. of quinolinecarboxamide derivs.)
- IT 49713-42-0P, Ethyl 4-hydroxy-8-iodo-3-quinolinecarboxylate
 58287-31-3P 103318-52-1P 188752-88-7P 228725-37-9P
 228725-72-2P 228725-85-7P 228726-33-8P 228726-41-8P
 228726-42-9P 228726-59-8P 228726-66-7P 228726-92-9P
 228726-93-0P 228728-08-3P 228728-23-2P, Ethyl
 4-hydroxy-6-iodoquinoline-3-carboxylate 228728-41-4P
 228728-42-5P 281651-90-9P 281651-91-0P 281651-92-1P
 281651-93-2P 281651-94-3P 281651-95-4P 281651-97-6P
 281651-98-7P 281651-99-8P 281652-02-6P 281652-03-7P
 281652-04-8P 281652-06-0P 281652-07-1P 281652-08-2P
 281652-09-3P 281652-12-8P 281652-13-9P 281652-14-0P
 281652-15-1P 281652-21-9P 281652-22-0P, 4-(4-
 Nitrobenzylidene)tetrahydro-2H-pyran 281652-23-1P 281652-24-2P
 281652-28-6P 281652-29-7P 281652-30-0P 281652-31-1P
 281652-32-2P 281652-33-3P 281652-34-4P 281652-35-5P
 281652-36-6P 281652-37-7P 281652-38-8P 281652-39-9P
 281652-41-3P 281652-42-4P 281652-44-6P 281652-45-7P
 281652-46-8P 281652-47-9P 281652-48-0P 281652-49-1P
 281652-50-4P 281652-51-5P 281652-52-6P 281652-53-7P
 281652-54-8P 281652-55-9P 281652-56-0P 281652-57-1P
 281652-59-3P 281652-60-6P 281652-61-7P 281652-62-8P
 281652-63-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)
 (intermediate, for prepn. of quinolinecarboxamide derivs. as
 antiviral agents)
- IT 281652-16-2P 281652-17-3P 281652-18-4P 281652-19-5P
 281652-20-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)
 (intermediate, for prepn. of quinolinethiocarboxamide derivs. as
 antiviral agents)
- IT 10341-26-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)
 (prepn. and hydride redn. to oxazepane)
- IT 2896-98-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)

(prepn. and hydride redn. to thiazepane)

IT 281650-73-5P 281650-90-6P 281650-91-7P 281650-93-9P
 281650-96-2P 281650-97-3P 281651-04-5P 281651-07-8P
 281651-22-7P 281651-25-0P 281651-26-1P 281651-31-8P
 281651-38-5P 281651-40-9P 281651-41-0P 281651-48-7P
 281651-65-8P 281651-70-5P 281651-76-1P 281651-82-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of quinolinecarboxamides as antiviral agents, esp. against herpes virus)

IT 281650-66-6P 281650-67-7P 281650-68-8P 281650-69-9P
 281650-70-2P 281650-71-3P 281650-72-4P 281650-74-6P
 281650-75-7P 281650-76-8P 281650-77-9P 281650-78-0P
 281650-79-1P 281650-80-4P 281650-81-5P 281650-82-6P
 281650-83-7P 281650-84-8P 281650-85-9P 281650-86-0P
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 281650-94-0P 281650-95-1P 281650-98-4P 281650-99-5P
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 281651-10-3P 281651-11-4P 281651-12-5P 281651-13-6P
 281651-14-7P 281651-15-8P 281651-16-9P 281651-17-0P
 281651-18-1P 281651-19-2P 281651-20-5P 281651-21-6P
 281651-23-8P 281651-24-9P 281651-27-2P 281651-28-3P
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 281651-60-3P 281651-61-4P 281651-62-5P 281651-63-6P
 281651-64-7P 281651-66-9P 281651-67-0P 281651-68-1P
 281651-69-2P 281651-71-6P 281651-72-7P 281651-73-8P
 281651-74-9P 281651-75-0P 281651-77-2P 281651-78-3P
 281651-79-4P 281651-80-7P 281651-81-8P 281651-83-0P
 281651-84-1P 281651-85-2P 281651-86-3P 281651-87-4P
 281651-88-5P 281651-89-6P 281652-43-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of quinolinecarboxamides as antiviral agents, esp. against herpes virus)

IT 281651-00-1P 281651-03-4P 281651-05-6P 281651-06-7P
 281651-56-7P 281652-64-0P 281652-65-1P 281652-66-2P
 281652-67-3P 281652-68-4P 281652-69-5P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of quinolinecarboxamides as antiviral agents, esp. against herpes virus)

IT 603-35-0, Triphenylphosphine, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (quaternization with nitrobenzyl bromide)

IT 78191-00-1, N-Methyl-N-methoxyacetamide
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction with bromofluorobenzylmorpholine)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN

10/026408

THE RE FORMAT

L8 ANSWER 5 OF 5 MARPAT COPYRIGHT 2003 ACS

(ALL HITS ARE ITERATION INCOMPLETES)

ACCESSION NUMBER: 129:95491 MARPAT

TITLE: Preparation of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivatives as Na⁺/H⁺ exchanger inhibitors

INVENTOR(S): Okazaki, Toshio; Kikuchi, Kazumi; Sugasawa, Keizo; Kaku, Hidetaka; Takanashi, Masahiro

PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan; Merck Patent G.m.b.H.; Kikuchi, Kazumi; Sugasawa, Keizo; Kaku, Hidetaka; Takanashi, Masahiro

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

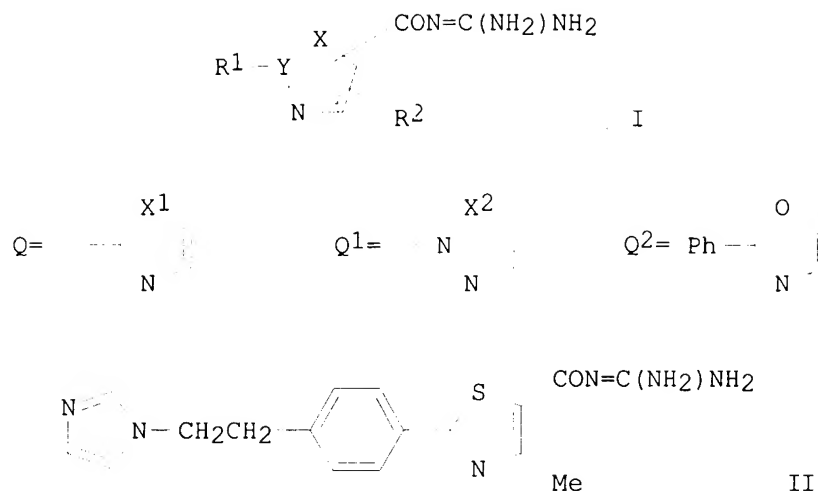
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9827061	A1	19980625	WO 1997-JP4605	19971215
W:	AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
ZA 9711102	A	19980813	ZA 1997-11102	19971210
AU 9854119	A1	19980715	AU 1998-54119	19971215
PRIORITY APPLN. INFO.:			JP 1996-335638	19961216
			WO 1997-JP4605	19971215

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AB N-[(Substituted five-membered heteroaryl)carbonyl]guanidine derivs. represented by general formula (I) or pharmacol. acceptable salts thereof [wherein the five-membered heteroaryl ring represents Q or Q1 (wherein X1 represents oxygen, sulfur, or NR3; and X2 represents nitrogen or CR4); R1 represents optionally substituted aryl or optionally substituted five- or six-membered monocyclic heteroaryl; R2 represents hydrogen, halogeno, optionally halogen-substituted lower alkyl, lower alkoxy, lower alkylthio, or optionally protected amino, provided that when the R1-substituted five-membered heteroaryl ring is Q2, R2 is neither hydrogen nor ethoxy; and R3 and R4 each represents hydrogen or optionally halogen-substituted lower alkyl] are prepd. They are useful as a drug, esp. an Na⁺/H⁺ exchanger inhibitor, for the prevention, treatment, or diagnosis of various diseases in which an Na⁺/H⁺ exchanger participates, such as hypertension, arrhythmia, angina pectoris, myocardial infarct, organ damages caused by ischemia or ischemic reperfusion, cell proliferative diseases (e.g. arteriosclerosis and cancer), and disorders caused by high blood sugar (e.g. complications of diabetes). Thus, imidazole was treated with NaH in DMF at room temp. for 30 min and then stirred with Et 2-[3-(2-bromoethoxy)phenyl]-4-methylthiazole-5-carboxylate at 70.degree. for 3 h followed by heating with guanidine hydrochloride in the presence of NaH at 80.degree. for 3 h to give the title compd., [(imidazolylmethoxy)phenyl]thiazolecarbonylguanidine deriv. (II). The title compds. I in vitro inhibited Na⁺/H⁺ exchanger with Ki of from 10⁻⁶ to 10⁻⁸.

IC ICM C07D231-14

ICS C07D231-38; C07D233-90; C07D249-10; C07D263-34; C07D277-24; C07D277-34; C07D453-02; A61K031-415; A61K031-42

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

ST imidazolylmethoxyphenylthiazolecarbonylguanidine prepn proton sodium exchanger inhibitor; thiazolecarbonylguanidine prepn proton sodium exchanger inhibitor; hypertension treatment
oxazolecarbonylguanidine; arrhythmia treatment
triazolecarbonylguanidine; angina pectoris treatment
triazolecarbonylguanidine; myocardial infarct treatment

- imidazolecarbonylguanidine; organ damage ischemia ischemic reperfusion; cell proliferative disease arteriosclerosis cancer; disorder high blood sugar complication diabetes; heteroarylcarbonylguanidine prepn antihypertensive; pyrazolecarbonylguanidine prepn antiarteriosclerotic
- IT Heart, disease
(angina pectoris; prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT Heart, disease
(arrhythmia; prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT Diabetes mellitus
(complications; prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT Cell proliferation
(disease; prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT Transport proteins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(hydrogen ion-sodium-exchanging; prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT Organ, animal
Organ, animal
(injury; prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT Reperfusion
(ischemic, organ damages caused by; prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT Ischemia
(organ damages caused by; prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT Antiarteriosclerotics
Antidiabetic agents
Antihypertensives
Antitumor agents
(prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger inhibitors for treatment of diseases)
- IT 209537-03-1P 209537-04-2P 209537-05-3P 209537-06-4P
209537-07-5P 209537-08-6P 209537-09-7P 209537-11-1P
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209538-78-3P	209538-80-7P	209540-12-5P	

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na+/H+ exchanger inhibitors for treatment of diseases)

IT 50-01-1, Guanidine hydrochloride 99-09-2, 3-Nitroaniline
 100-39-0, Benzyl bromide 109-54-6, 3-(Dimethylamino)propyl
 chloride 109-64-8, 1,3-Dibromopropane 110-52-1,
 1,4-Dibromobutane 118-90-1, o-Methylbenzoic acid 124-40-3,
 Dimethylamine, reactions 141-97-9, Ethyl acetoacetate 288-32-4,
 Imidazole, reactions 363-58-6, Ethyl 2-chloro-4,4,4-
 trifluoroacetoacetate 459-57-4, p-Fluorobenzaldehyde 501-53-1,
 Benzyl chloroformate 536-90-3, 3-Methoxyaniline 609-15-4, Ethyl
 2-chloroacetoacetate 625-36-5, 3-Chloropropionyl chloride
 873-62-1, m-Cyanophenol 4637-24-5 5407-04-5 6214-65-9,
 5-Acetyluracil 7333-63-3, (4-Bromobutyl)triphenylphosphonium
 bromide 18355-96-9, 3-(Dimethylamino)propyltriphenylphosphonium
 bromide 20691-89-8, 1-Methylpiperidine-4-methanol 24252-37-7
 24964-64-5, 3-Cyanobenzaldehyde 26628-22-8, Sodium azide
 39232-91-2, 3-Methoxyphenylhydrazine hydrochloride 51516-96-2,
 3-Nitrophenylhydrazine hydrochloride 63888-94-8 209540-05-6
 209540-06-7 209540-08-9 209540-09-0 209540-10-3

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of N-[(substituted five-membered heteroaryl)carbonyl]guanidine derivs. as Na+/H+ exchanger inhibitors for treatment of diseases)

IT 20954-27-2P 24723-35-1P 61147-43-1P, 3-(Benzyloxy)benzonitrile
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 209539-24-2P 209539-25-3P 209539-26-4P 209539-27-5P
 209539-28-6P 209539-29-7P 209539-31-1P 209539-32-2P
 209539-33-3P 209539-34-4P 209539-36-6P 209539-37-7P
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10/026408

209539-43-5P	209539-44-6P	209539-45-7P	209539-46-8P
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209539-62-8P	209539-63-9P	209539-64-0P	209539-65-1P
209539-66-2P	209539-67-3P	209539-69-5P	209539-70-8P
209539-71-9P	209539-72-0P	209539-73-1P	209539-74-2P
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209539-80-0P	209539-81-1P	209539-83-3P	209539-84-4P
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209540-00-1P	209540-01-2P	209540-02-3P	209540-03-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)

(prepn. of N-[(substituted five-membered
heteroaryl)carbonyl]guanidine derivs. as Na⁺/H⁺ exchanger
inhibitors for treatment of diseases)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN
THE RE FORMAT

FILE 'MARPATPREV' ENTERED AT 12:55:12 ON 14 FEB 2003

L1 STR

15
Cb

NH 14

13 C O
18
NH 12

HO2C -C C 11 10
17 16 O

2	Cb	NH	SO2	Cb	NH	C	NH	C
	3	4	5	6	7	8	9	

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 2
GGCAT IS UNS AT 5
GGCAT IS UNS AT 15
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

MLEVEL IS CLASS ON RING NODES AND RING GROUPS
MLEVEL IS CLASS ON CHAIN NODES AND CHAIN GROUPS
ECLEVEL IS LIM ON ALL NODES

10/026408

ALL RING(S) ARE ISOLATED

L9 0 SEA FILE=MARPATPREV SSS FUL L1 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 52 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.03

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10/026408

(FILE 'REGISTRY' ENTERED AT 12:45:59 ON 14 FEB 2003)
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NH 14
13 C O
18
NH 12
HO2C C C 11 10
17 16 O
2 Cb NH SO2 Cb NH C NH C
3 4 5 6 7 8 9

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 2
GGCAT IS UNS AT 5
GGCAT IS UNS AT 15
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
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SEARCH TIME: 00.00.01

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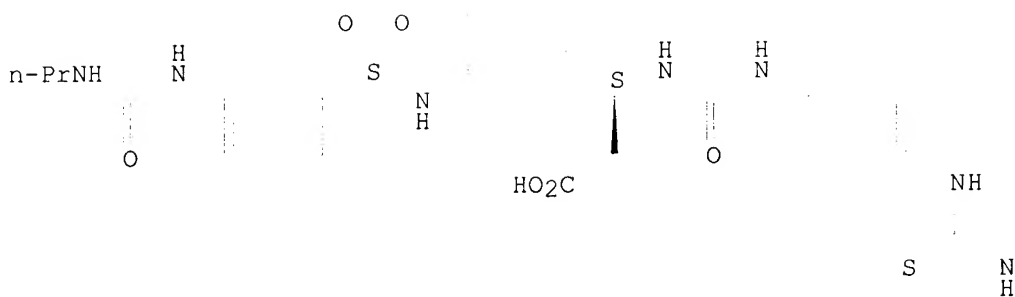
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E1 THROUGH E48 ASSIGNED

L4 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:693123 HCAPLUS
DOCUMENT NUMBER: 137:210930
TITLE: Enzyme-activated cytostatic conjugates with
integrin ligands
INVENTOR(S): Lerchen, Hans-georg; Baumgarten, Joerg; Schoop,
Andreas; Albers, Markus
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 72 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

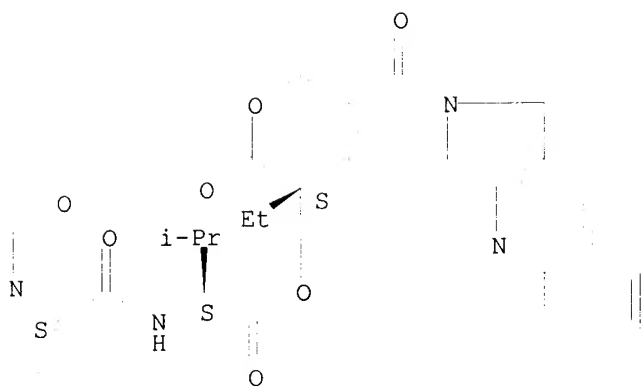
PATENT NO. KIND DATE APPLICATION NO. DATE

Searcher : Shears 308-4994

Absolute stereochemistry.



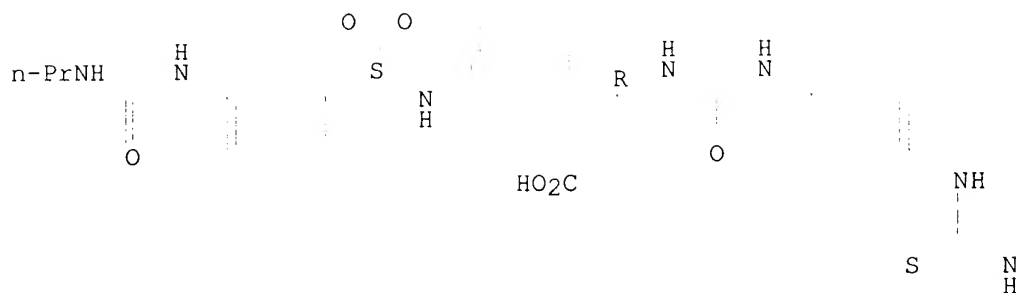
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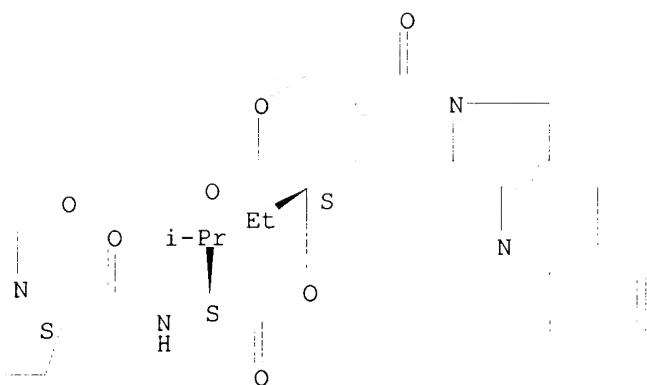
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 no]carbonyl]amino]phenyl]amino]thioxomethyl]glycyl-L-prolyl-,
 3-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-
 pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester, monosodium
 salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Searcher : Shears 308-4994



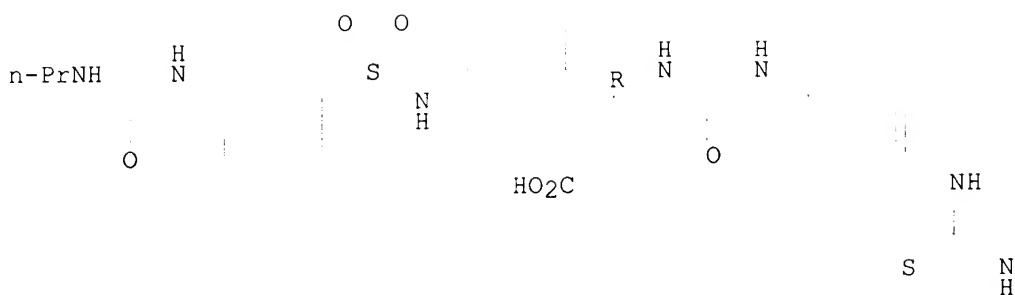
● Na



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 no]carbonyl]amino]phenyl]amino]thioxomethyl]-L-alanyl-L-prolyl-,
 3-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-
 pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester, monosodium
 salt (9CI) (CA INDEX NAME)

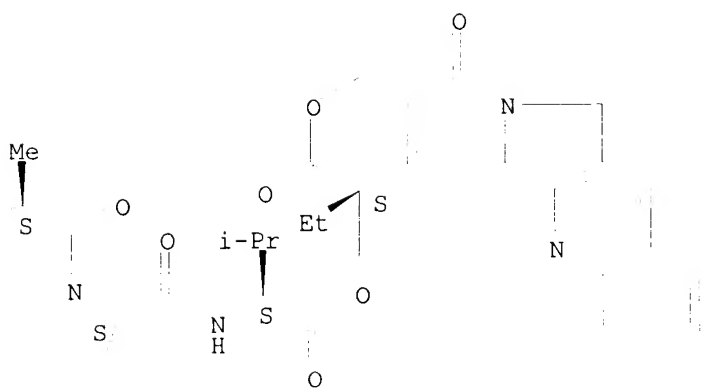
Absolute stereochemistry.

PAGE 1-A



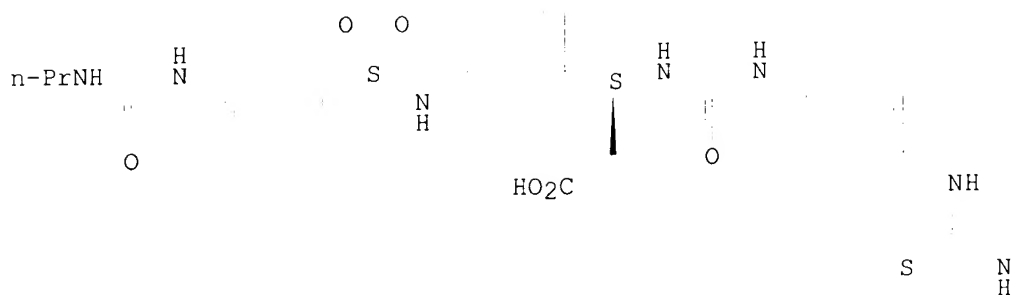
● Na

PAGE 1-B

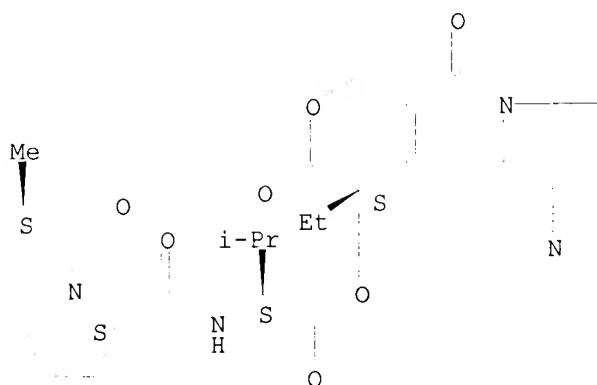


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Absolute stereochemistry.



● Na



IT 455940-58-6P 455940-60-0P

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(enzyme-activated cytostatic conjugates with integrin ligands which can be selectively cleaved by elastase in relation to toxicity to hemopoietic stem cells)

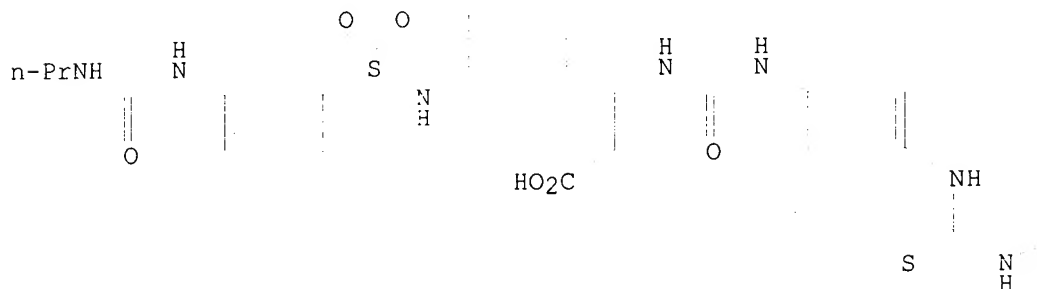
RN 455940-58-6 HCAPLUS

CN L-Valine, N2-[[[4-[[[2-carboxy-1-[3-[[[3-[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]phenyl]ethyl]amino]carbonyl]amino]phenyl]amino]thioxomethyl]-L-asparaginy]-L-prolyl-

, 3-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester, monosodium salt (9CI) (CA INDEX NAME)

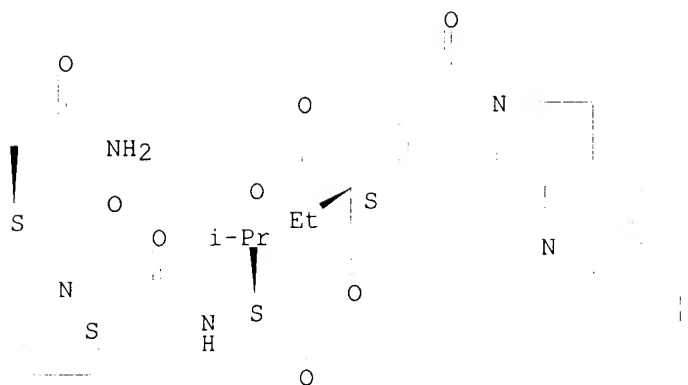
Absolute stereochemistry.

PAGE 1-A



● Na

PAGE 1-B



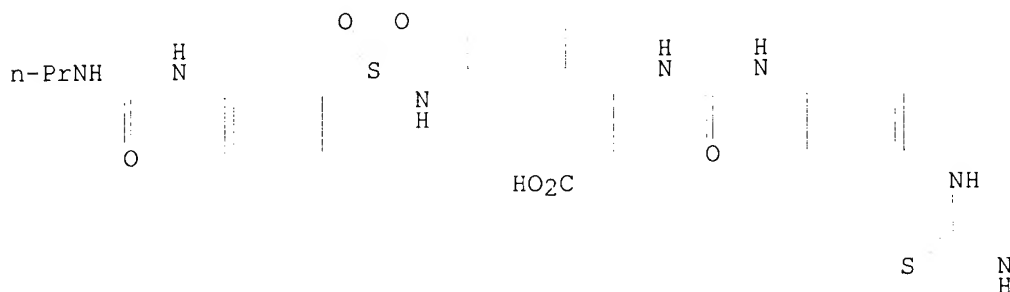
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 3-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-

10/026408

pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester, monosodium
salt (9CI) (CA INDEX NAME)

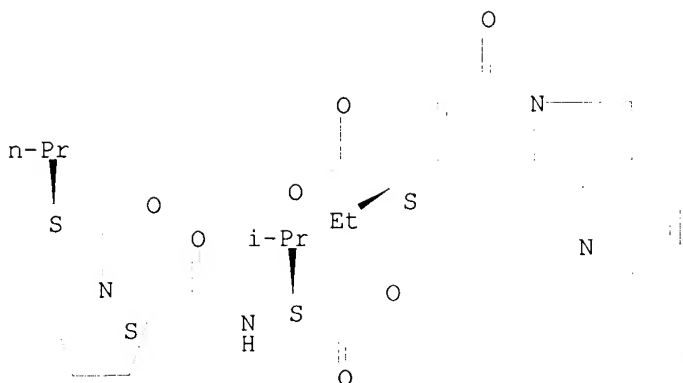
Absolute stereochemistry.

PAGE 1-A



● Na

PAGE 1-B



IT 455940-55-3P 455940-63-3P 455940-65-5P
455940-67-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

(enzyme-activated cytostatic conjugates with integrin ligands)

Searcher : Shears 308-4994

10/026408

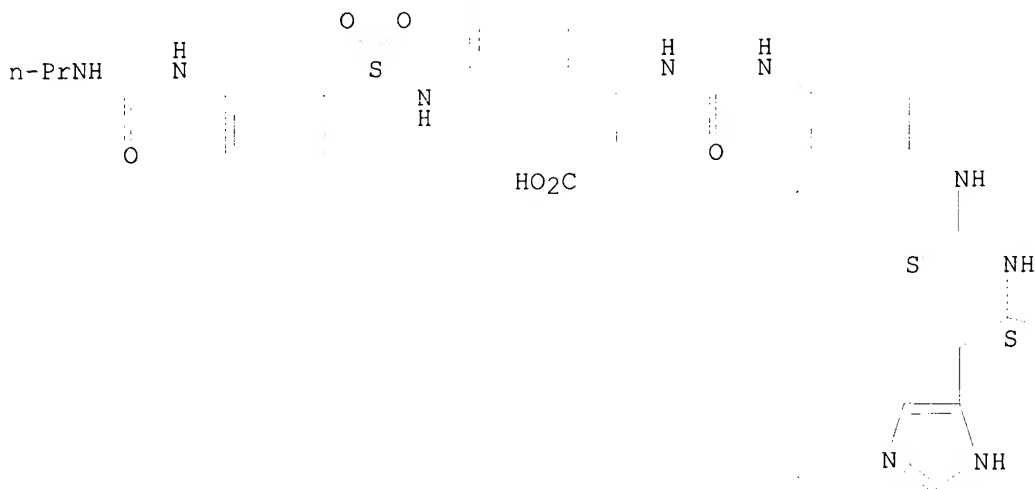
which can be selectively cleaved by elastase in relation to toxicity to hemopoietic stem cells)

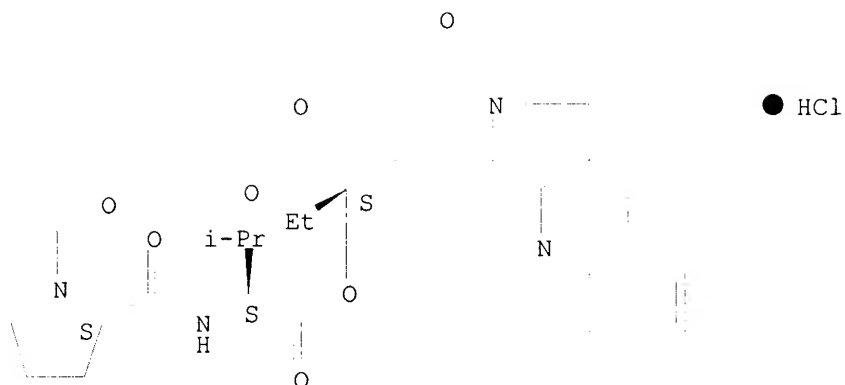
RN 455940-55-3 HCAPLUS

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 3-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-
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 monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

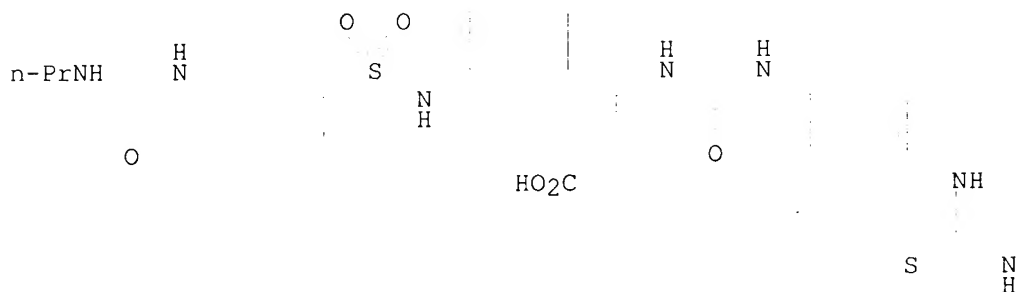
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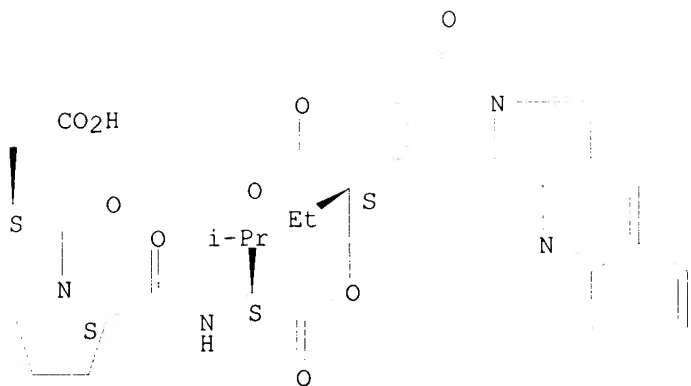




RN 455940-63-3 HCAPLUS
 CN L-Valine, N-[[[4-[[[2-carboxy-1-[3-[[[3-
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 no]carbonyl]amino]phenyl]amino]thioxomethyl]-L-.alpha.-aspartyl-L-
 prolyl-, 3-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-
 pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester (9CI) (CA
 INDEX NAME)

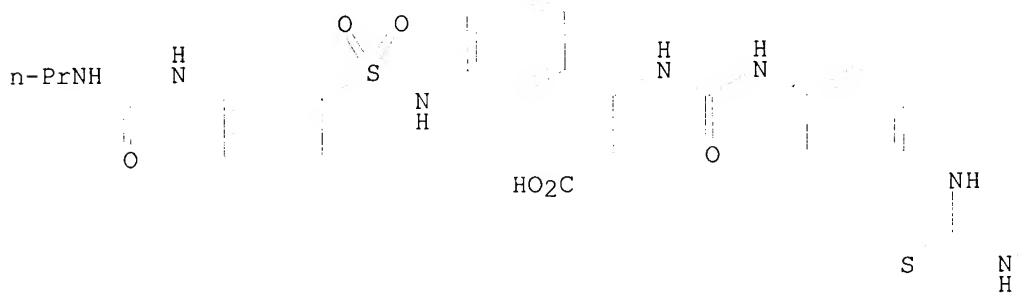
Absolute stereochemistry.

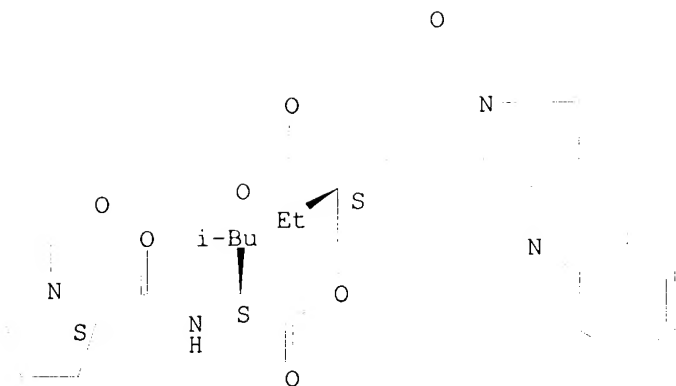




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 3-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-
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 INDEX NAME)

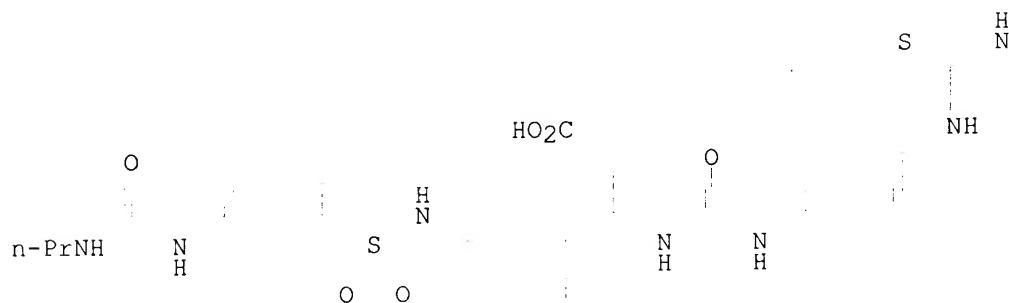
Absolute stereochemistry.

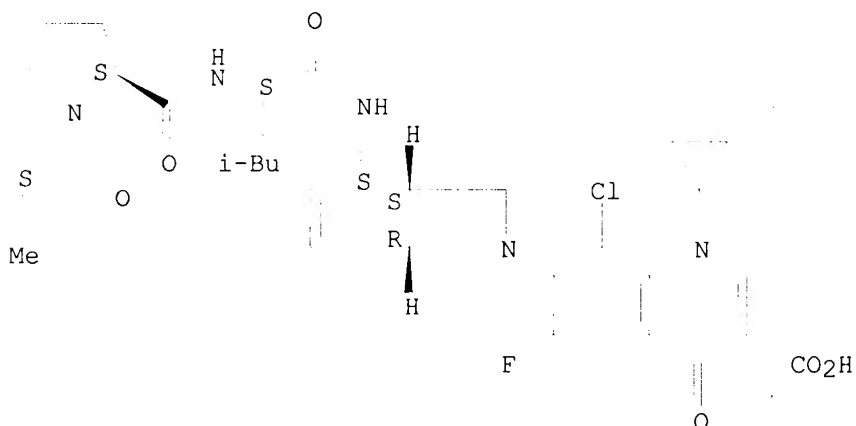




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 no] carbonyl] amino] phenyl] amino] thioxomethyl]-L-alanyl-L-prolyl-N-
 [(3aS,4S,7aR)-2-(3-carboxy-8-chloro-1-cyclopropyl-6-fluoro-1,4-
 dihydro-4-oxo-7-quinolinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-
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Absolute stereochemistry.

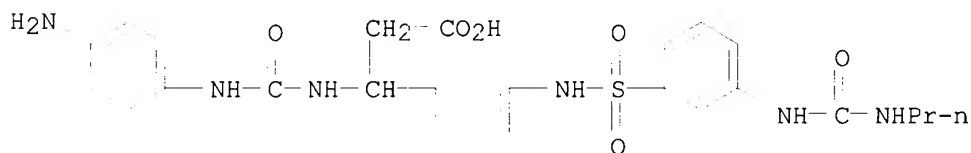




IT 330155-52-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)(enzyme-activated cytostatic conjugates with integrin ligands
which can be selectively cleaved by elastase in relation to
toxicity to hemopoietic stem cells)

RN 330155-52-7 HCAPLUS

CN Benzenepropanoic acid, .beta.-[[[(4-aminophenyl)amino]carbonyl]amino
]-3-[[[3-[[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]- (9CI)
(CA INDEX NAME)REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN
THE RE FORMAT

L4 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:503334 HCAPLUS

DOCUMENT NUMBER: 137:63479

TITLE: Preparation of conjugates of integrin receptor
antagonists and a cytostatic agent having
specifically cleavable linking unitsINVENTOR(S): Lerchen, Hans-Georg; Baumgarten, Joerg;
Lockhoff, Oswald; Albers, Markus; Schoop,
Andreas

PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany

SOURCE: Eur. Pat. Appl., 127 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1219305	A1	20020703	EP 2000-128401	20001227
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WO 2002051444	A1	20020704	WO 2001-EP14965	20011218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002183256	A1	20021205	US 2001-26408	20011221
PRIORITY APPLN. INFO.:			EP 2000-128401	A 20001227
OTHER SOURCE(S):			MARPAT 137:63479	
AB	<p>The invention relates to cytostatics CT-LI-Sp-IA [CT denotes a cytotoxic radical or a radical of a cytostatic or a cytostatic deriv. which can addnl. carry a hydroxy, carboxy or amino group; LI is a linker group comprising 5- to 8-amino acid residues in the D- or L-configuration, which can each optionally carry protective groups; Sp is absent or a carbonyl or thiocarbonyl radical; IA is a non-peptide radical addressing an .alpha.v.beta.3 integrin receptor, e.g., a radical of formula R18COCH2CHPhNHCCH2NHCO-m-C6H4NH[C(:NH)NHR19]q, where R18 is OH, (un)substituted (cyclo)alkoxy, aryloxy, heterocyclyloxy, a direct bond, or an atom from the group N, O and S, via which the radical is bonded to the rest of the conjugate; q is 0 or 1; R19 is H, (un)substituted (cyclo)alkyl, aryl, heterocyclyl, an alkylamine or alkylamide radical, or a direct bond, via which the radical is bonded to the rest of the conjugate] and their physiol. acceptable salts and stereoisomers. The cytostatics have a tumor-specific action as a result of linkage to .alpha.v.beta.3 integrin antagonists via preferred linking units which can be selectively cleaved by enzymes such as metallo matrix proteases (MMPs5), i.e., by enzymes which can esp. be found in tumor tissue. The preferred linking units guarantee the serum stability of the conjugate of cytostatic and .alpha.v.beta.3 integrin antagonist and, at the same time, the desired intracellular action within tumor cells as a result of its specific enzymic or hydrolytic cleavability with release of the cytostatic. Thus, 20-O-[PrNHCONH-m-C6H4SO2NH-m-C6H4CH(CH2CO2H)NHCONH-p-C6H4NHC(S)-Pro-Leu-Gly-Leu-His-Val]camptothecin (1) was prepd. by reaction of 20(S)-camptothecin with N-(tert-butoxycarbonyl)-L-valine-N-carboxyanhydride, deprotection, peptide coupling reactions, and formation of the thiourea linkage. Compd. 1 was assayed for cytostatic action on human large intestine cell line HT29 (IC50 = 40 nM).</p>			
IT	<p>439864-66-1P 439864-67-2P 439864-68-3P 439864-71-8P 439864-73-0P 439864-74-1P 439864-75-2P 439864-76-3P 439864-77-4P 439864-78-5P 439864-79-6P 439864-80-9P 439864-81-0P 439864-82-1P 439864-83-2P 439864-84-3P 439864-85-4P 439864-86-5P</p>			

439864-87-6P 439864-88-7P 439864-89-8P
 439864-90-1P 439864-91-2P 439864-92-3P
 439864-93-4P 439864-94-5P 439864-95-6P
 439864-96-7P 439864-97-8P 439864-98-9P
 439864-99-0P 439865-00-6P 439865-01-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

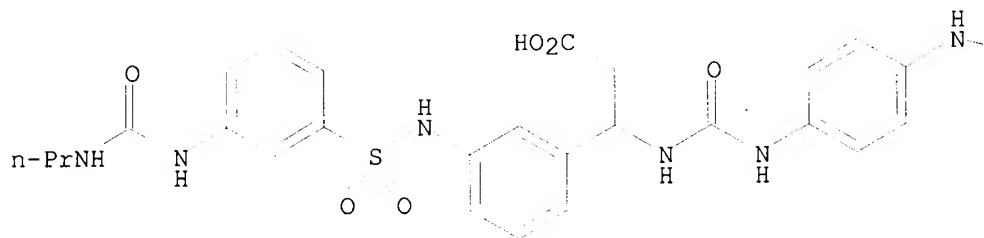
(prepn. of conjugates of integrin receptor antagonists and a cytostatic agent having specifically cleavable linking units)

RN 439864-66-1 HCAPLUS

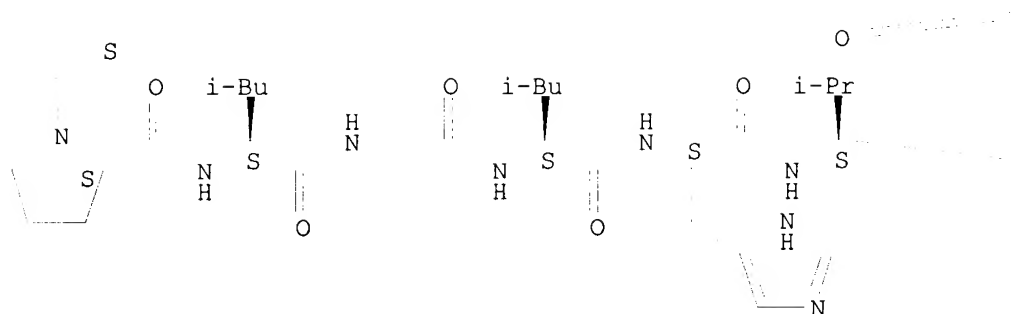
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Absolute stereochemistry.

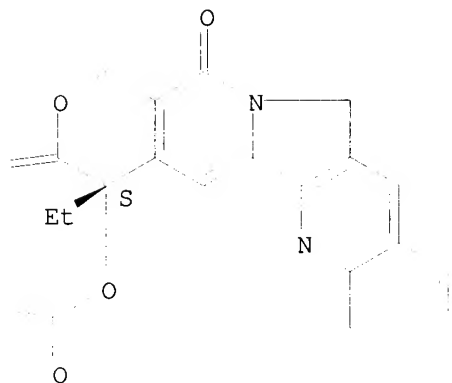
PAGE 1-A



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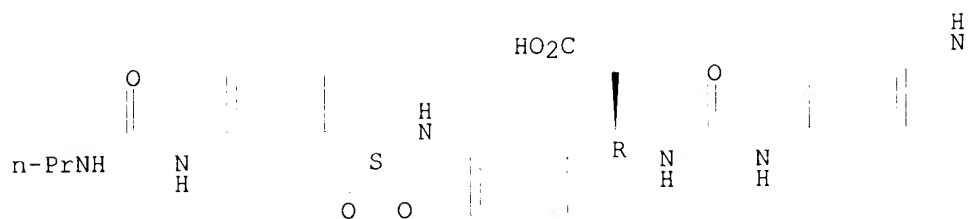


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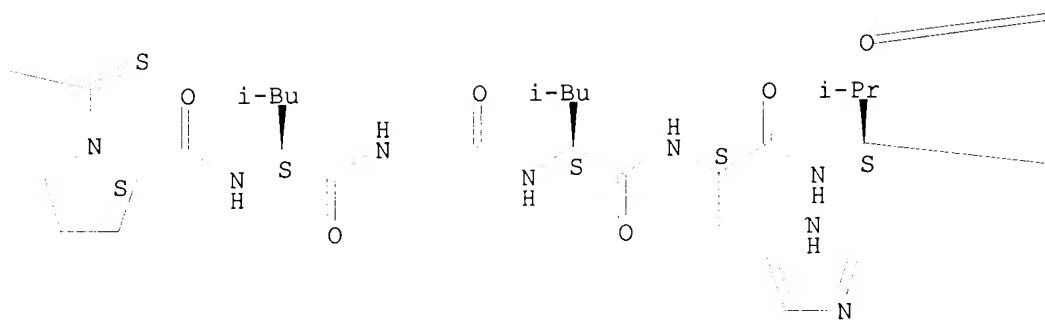
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 (9CI) (CA INDEX NAME)

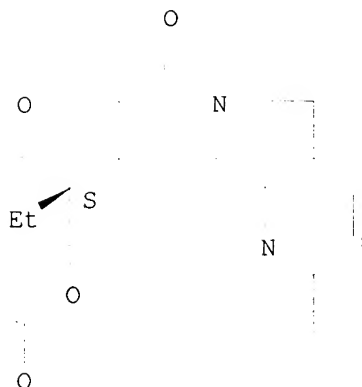
Absolute stereochemistry.

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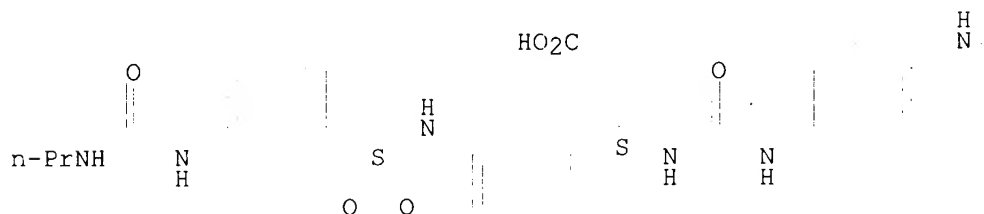




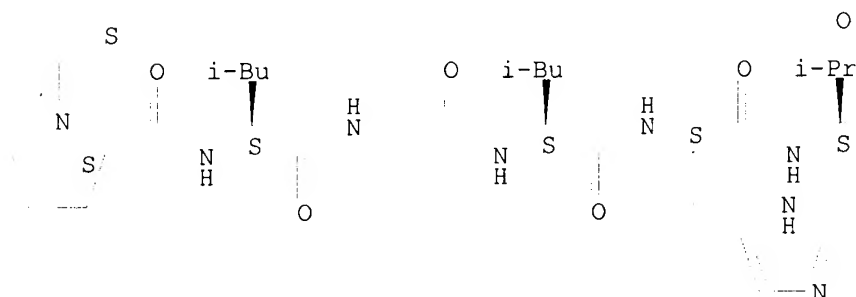
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 (9CI) (CA INDEX NAME)

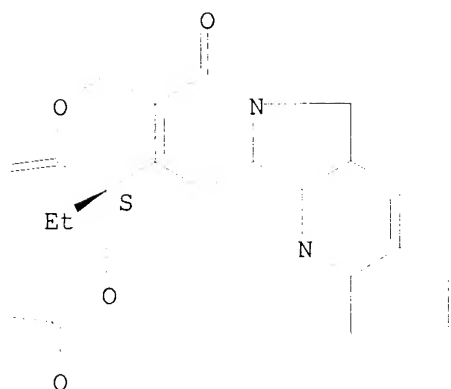
Absolute stereochemistry.



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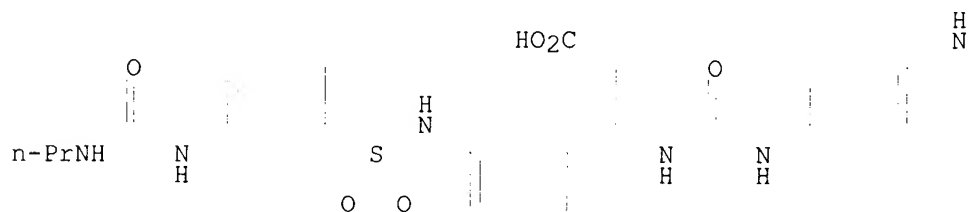
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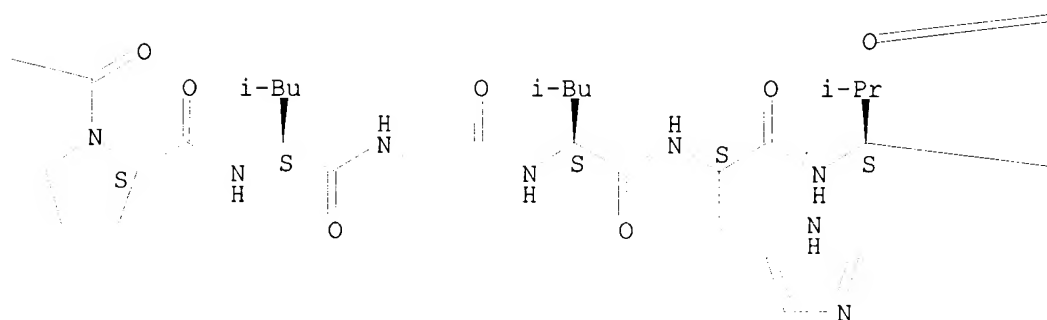
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 leucyl-L-histidyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-
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 INDEX NAME)

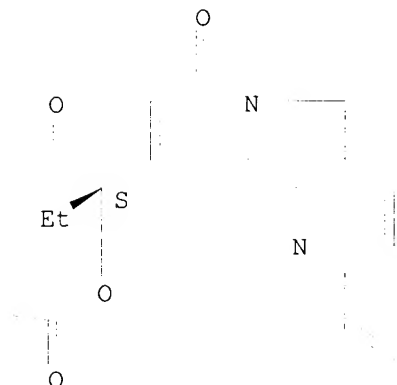
Absolute stereochemistry.

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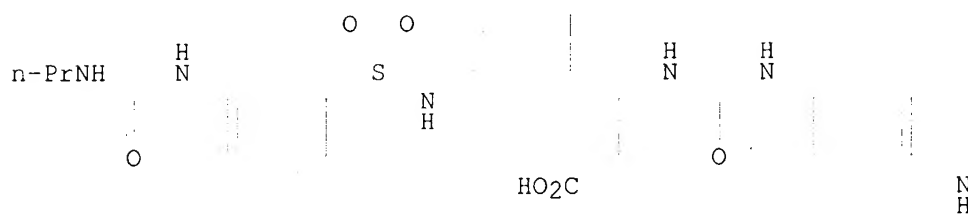




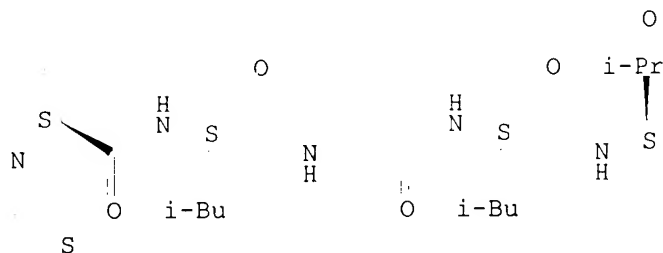
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 INDEX NAME)

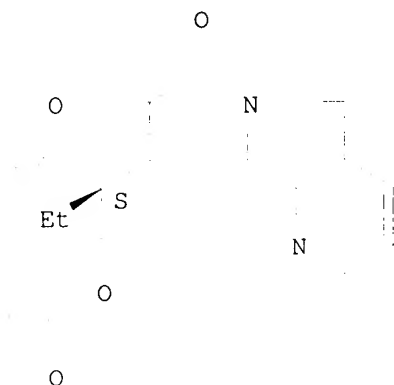
Absolute stereochemistry.



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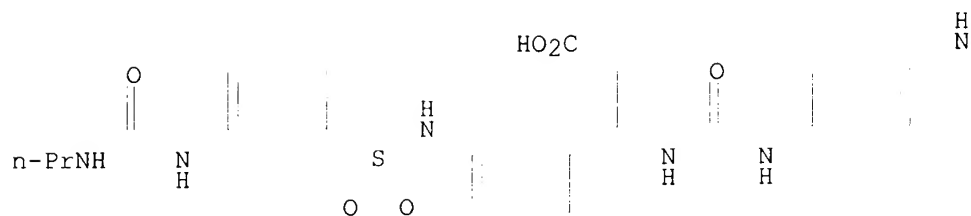
PAGE 1-C



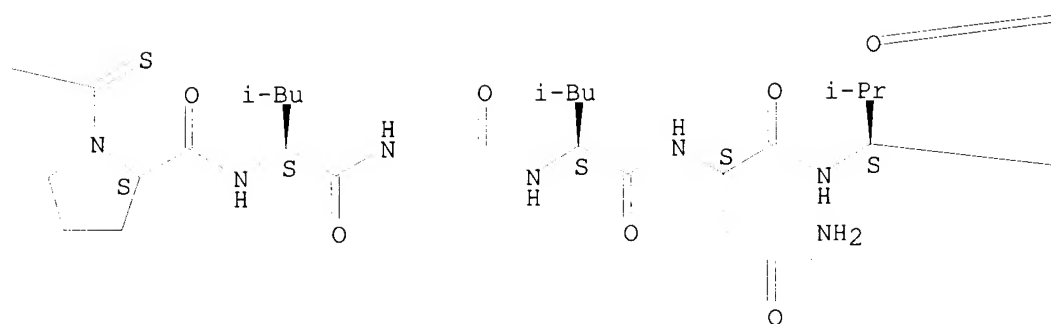
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 L-leucyl-L-asparaginyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-
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 (9CI) (CA INDEX NAME)

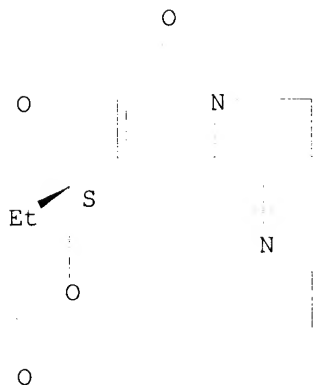
Absolute stereochemistry.

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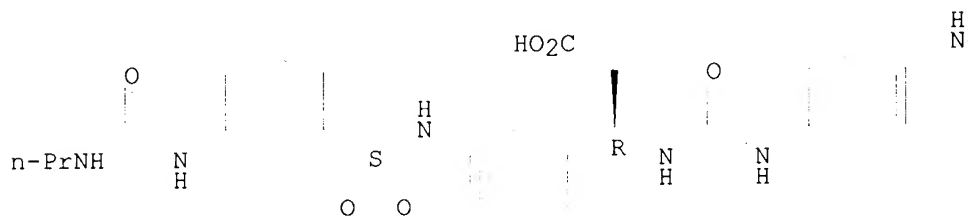
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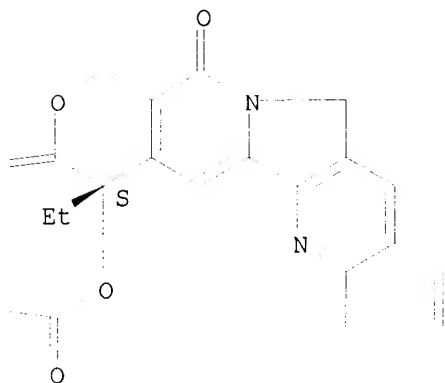
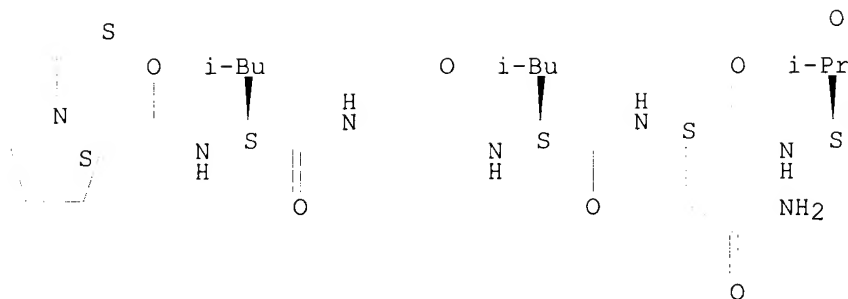




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Absolute stereochemistry.

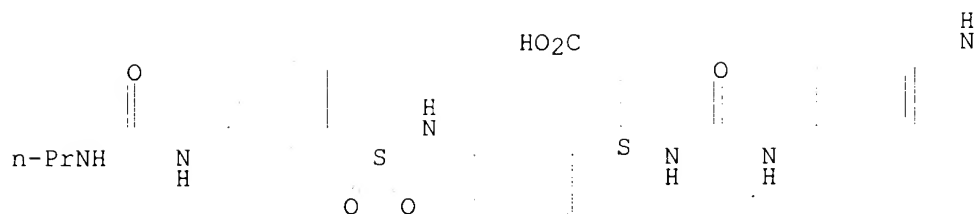




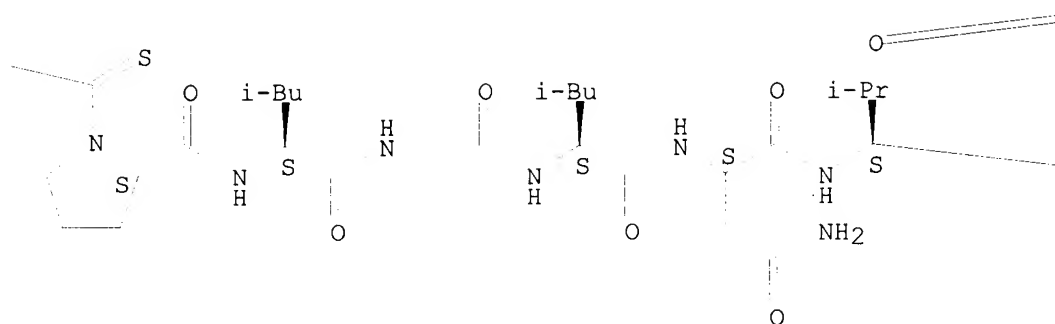
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 L-leucyl-L-asparaginy]-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-
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 (9CI) (CA INDEX NAME)

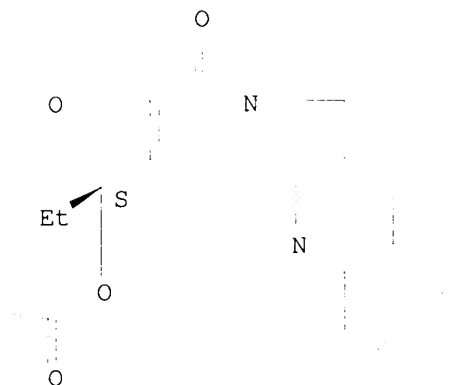
Absolute stereochemistry.

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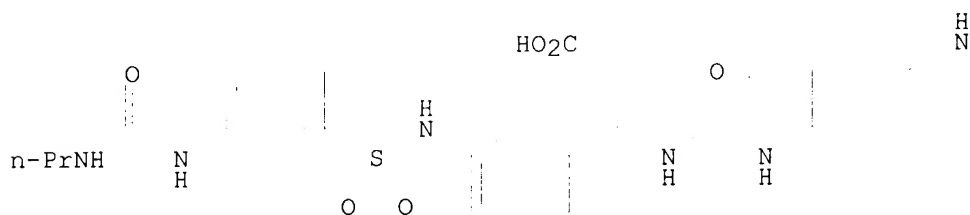
PAGE 1-B



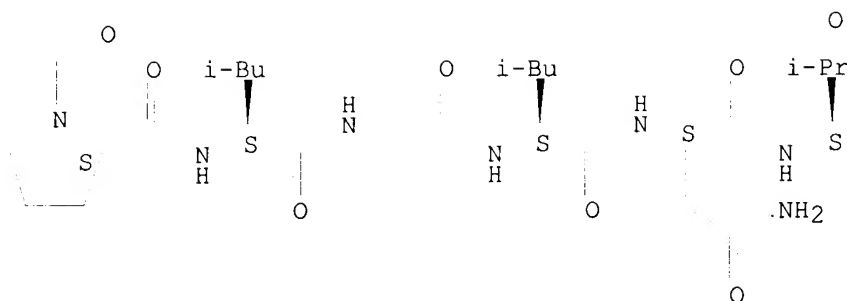


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 (9CI) (CA INDEX NAME)

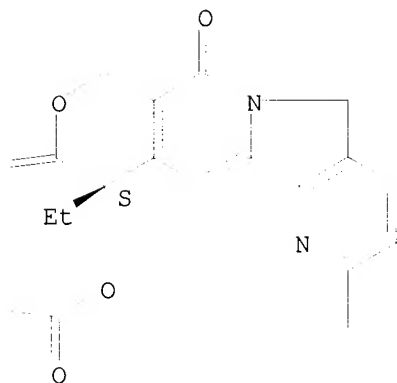
Absolute stereochemistry.



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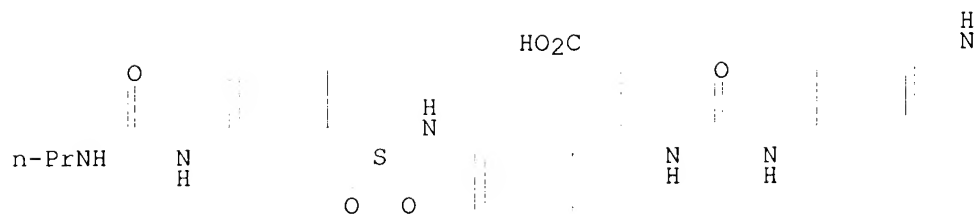


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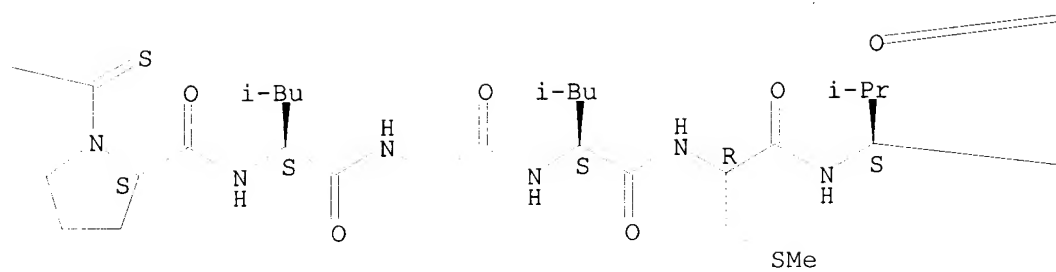
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 L-leucyl-S-methyl-L-cysteinyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-
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 (9CI) (CA INDEX NAME)

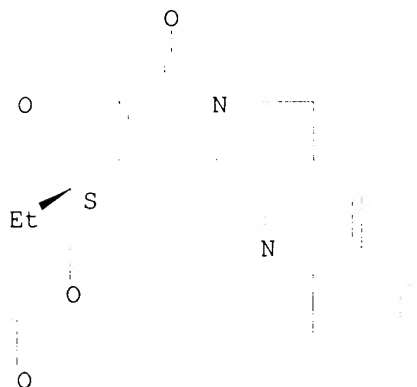
Absolute stereochemistry.

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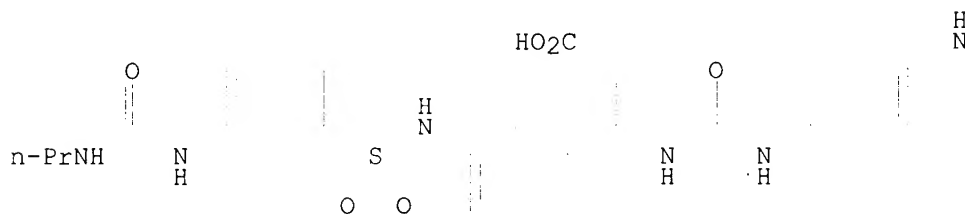




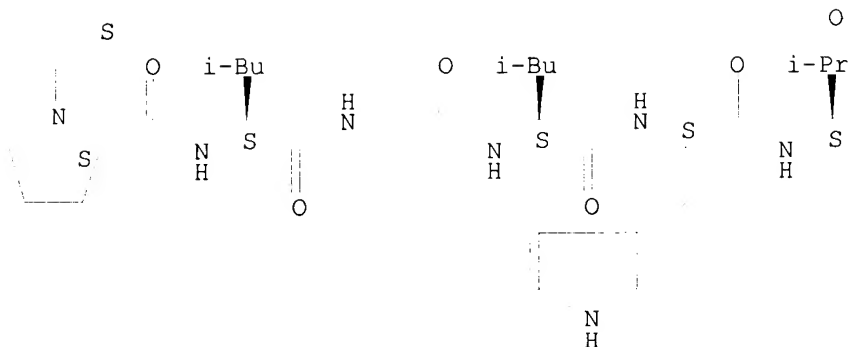
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 (9CI) (CA INDEX NAME)

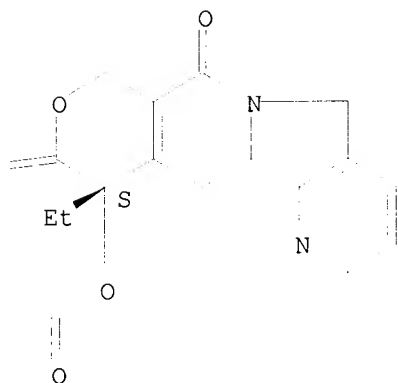
Absolute stereochemistry.



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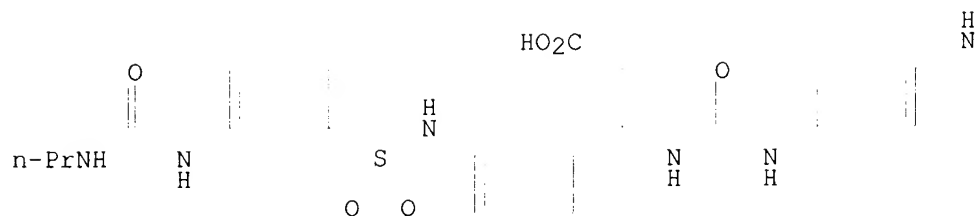
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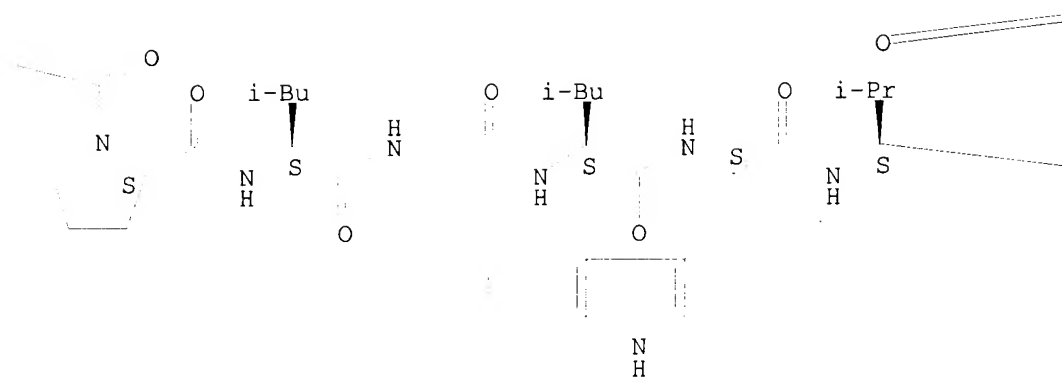
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 (9CI) (CA INDEX NAME)

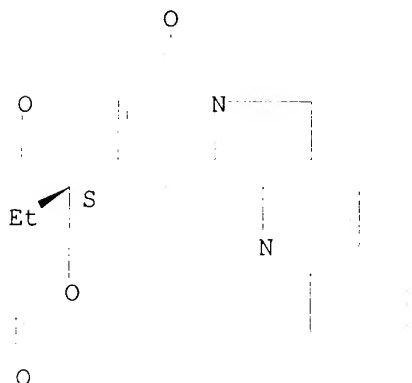
Absolute stereochemistry.

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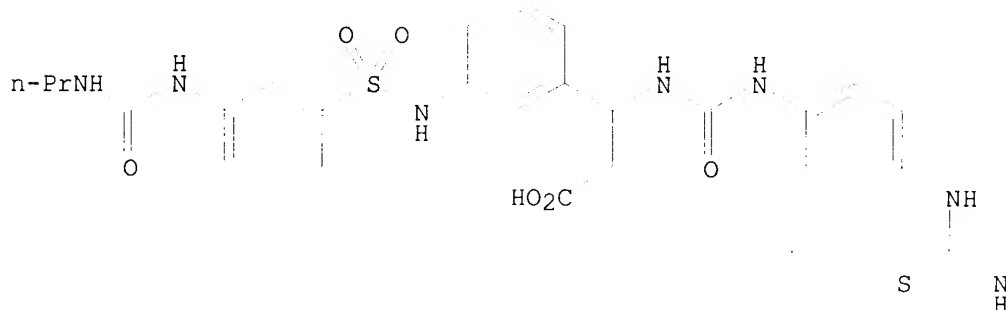


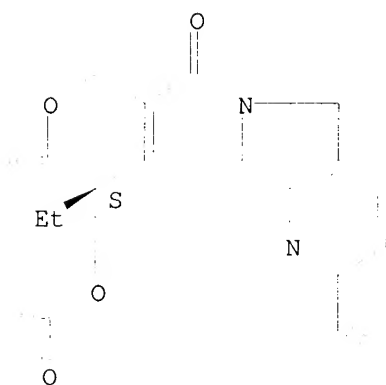
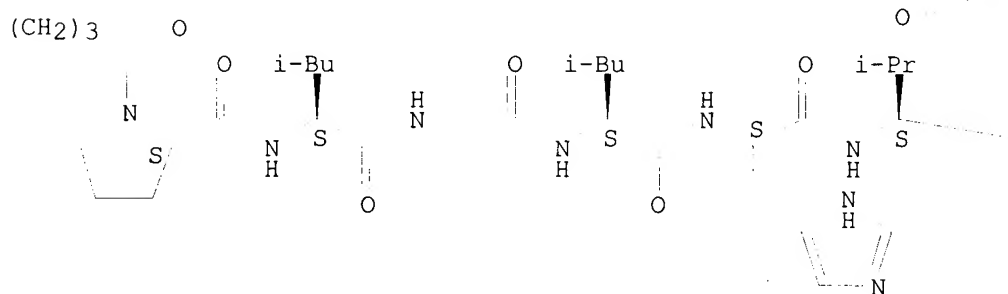


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 3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-
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Absolute stereochemistry.

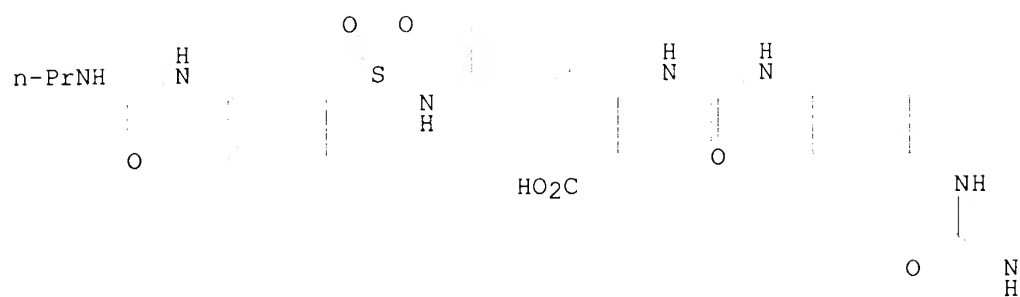




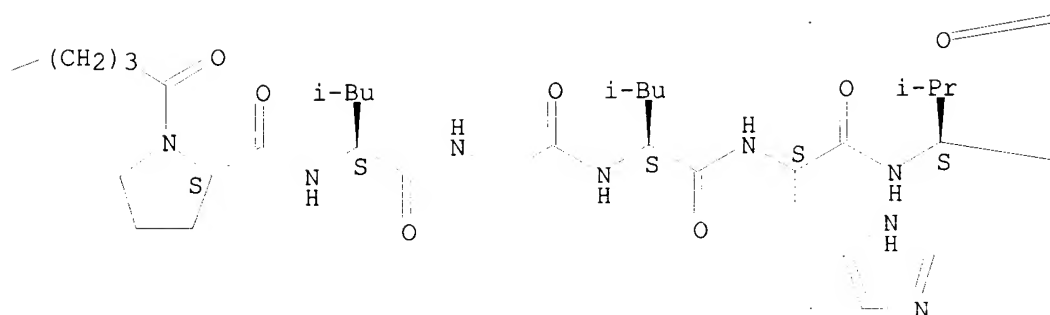
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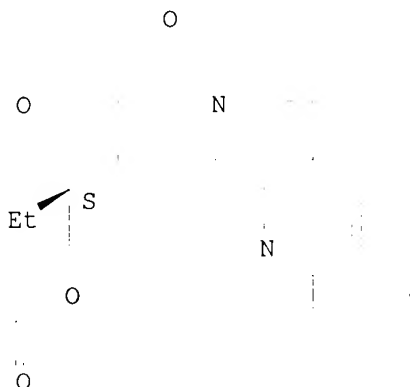
Absolute stereochemistry.

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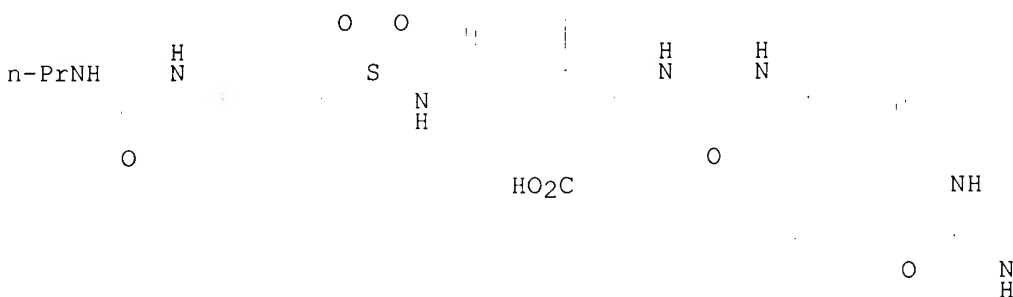
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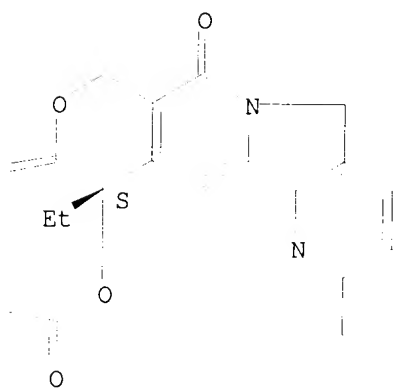
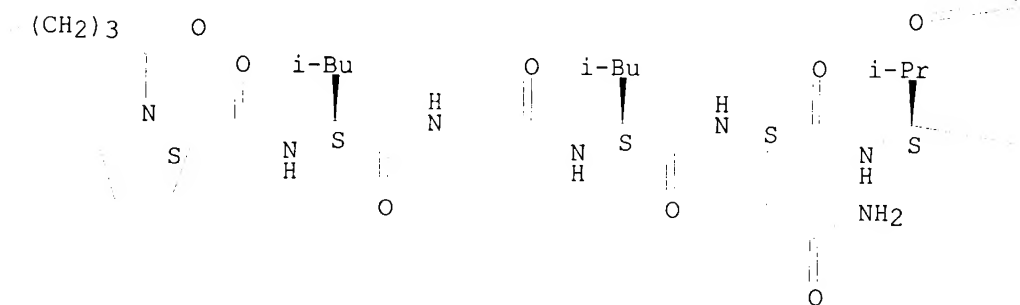




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 L-leucylglycyl-L-leucyl-L-asparaginy]-, 6-[(4S)-4-ethyl-3,4,12,14-
 tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-
 4-yl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



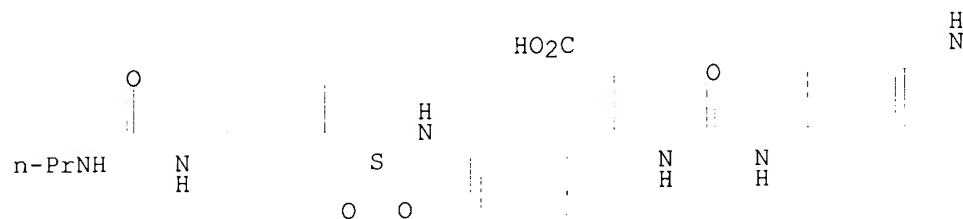


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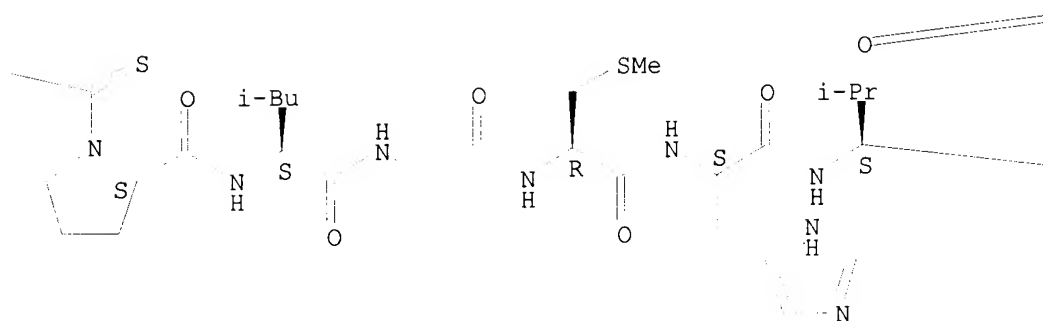
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 S-methyl-L-cysteinyl-L-histidyl-, 6-[(4S)-4-ethyl-3,4,12,14-
 tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-
 4-yl] ester (9CI) (CA INDEX NAME)

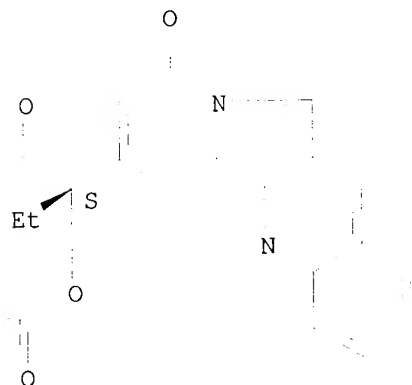
Absolute stereochemistry.

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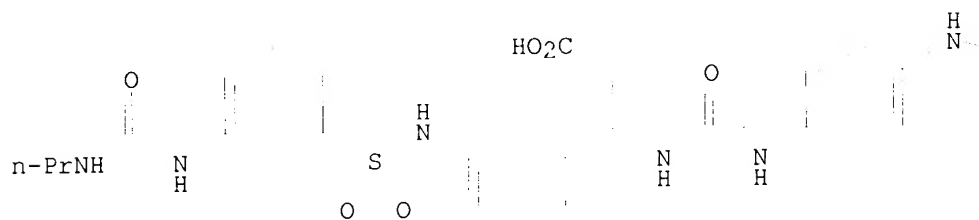
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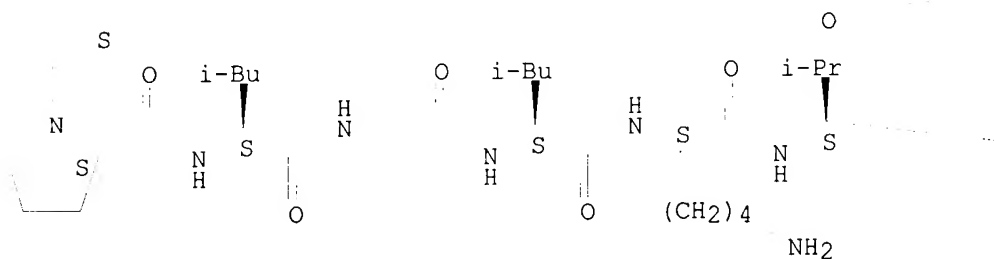


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 no]carbonyl]amino]phenyl]amino]thioxomethyl]-L-prolyl-L-leucylglycyl-
 L-leucyl-L-lysyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-
 1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester (9CI) (CA
 INDEX NAME)

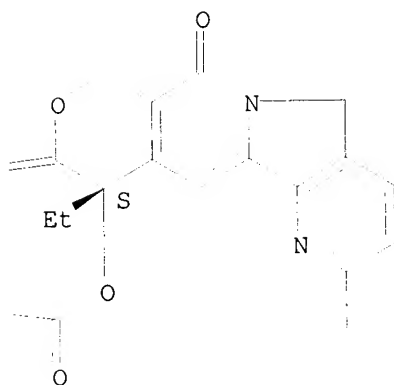
Absolute stereochemistry.



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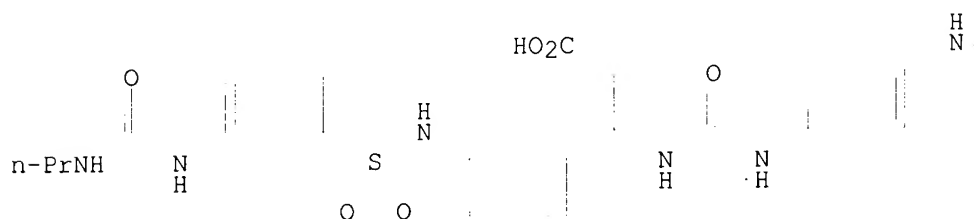


RN 439864-86-5 HCAPLUS

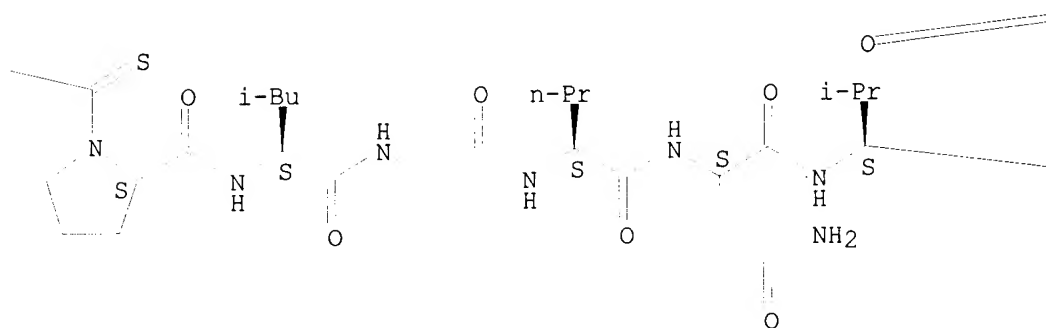
CN L-Valine, 1-[[[4-[[[2-carboxy-1-[3-[[[3-
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 no]carbonyl]amino]phenyl]amino]thioxomethyl]-L-prolyl-L-leucylglycyl-
 L-norvalyl-L-asparaginyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-
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 (9CI) (CA INDEX NAME)

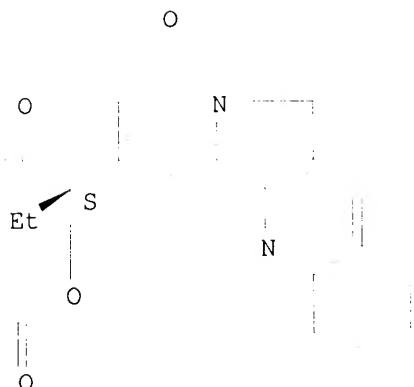
Absolute stereochemistry.

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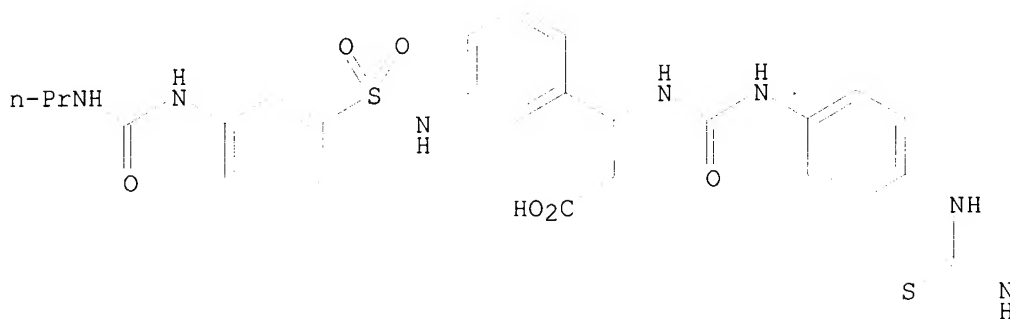


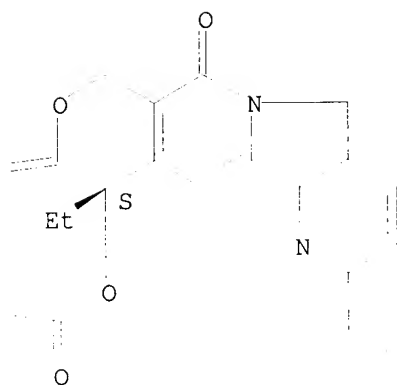
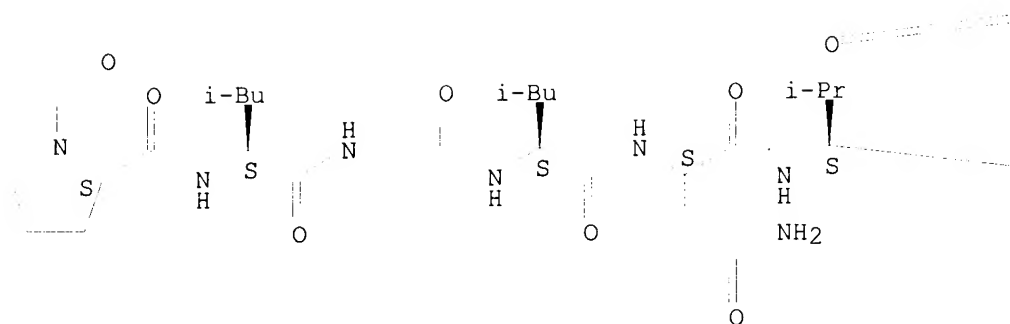


RN 439864-87-6 HCAPLUS

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 [(propylamino) carbonyl] amino] phenyl] sulfonyl] amino] phenyl] ethyl] ami
 no] carbonyl] amino] phenyl] amino] thioxomethyl] glycyl-L-prolyl-L-
 leucylglycyl-L-leucyl-L-asparaginyl-, 7-[(4S)-4-ethyl-3,4,12,14-
 tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-
 4-yl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

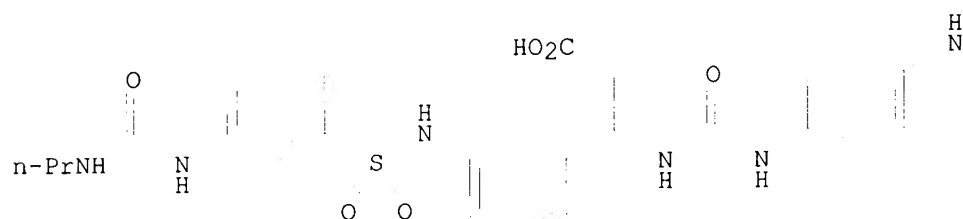




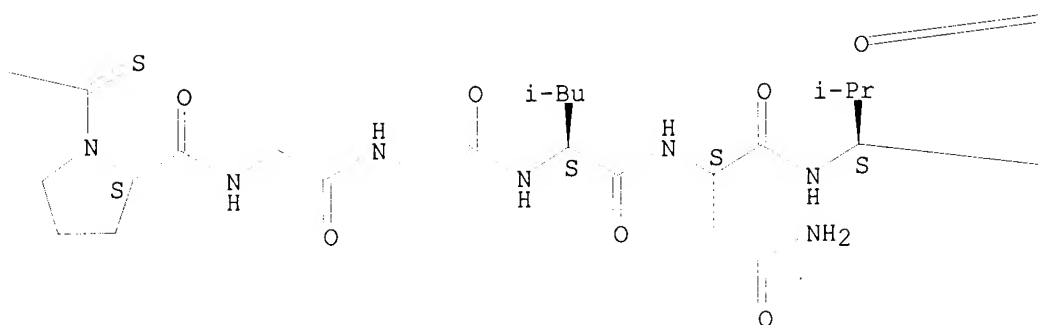
RN 439864-88-7 HCAPLUS
 CN L-Valine, 1-[[[4-[[[2-carboxy-1-[3-[[[3-
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 leucyl-L-asparaginyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-
 dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester
 (9CI) (CA INDEX NAME)

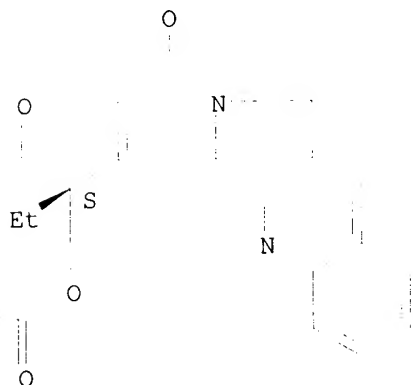
Absolute stereochemistry.

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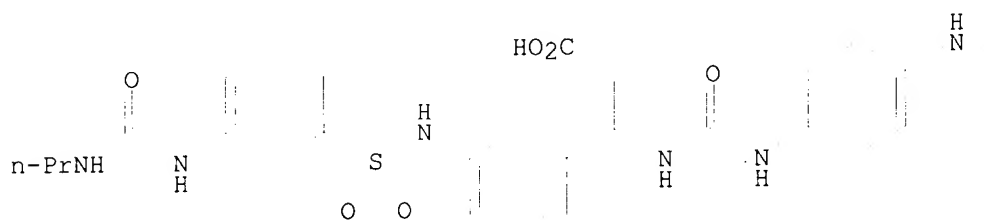
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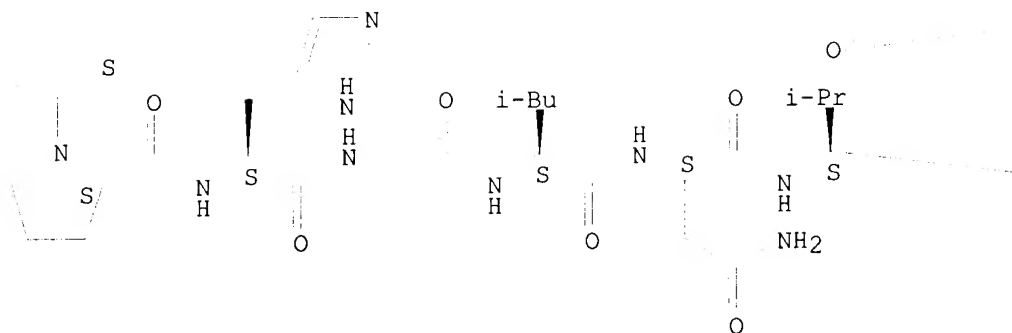


RN 439864-89-8 HCAPLUS
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 no]carbonyl]amino]phenyl]amino]thioxomethyl]-L-prolyl-L-
 histidylglycyl-L-leucyl-L-asparaginy]-, 6-[(4S)-4-ethyl-3,4,12,14-
 tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-
 4-yl] ester (9CI) (CA INDEX NAME)

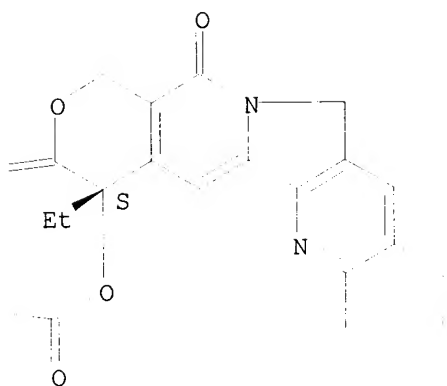
Absolute stereochemistry.



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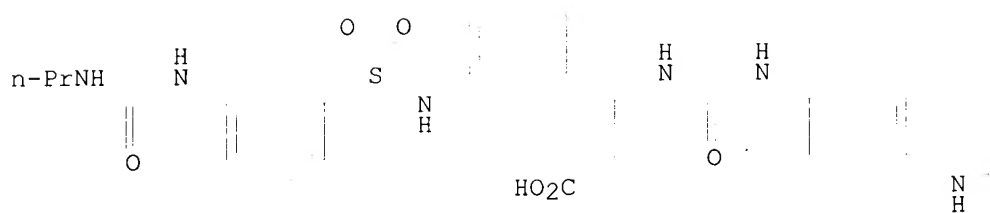


RN 439864-90-1 HCAPLUS

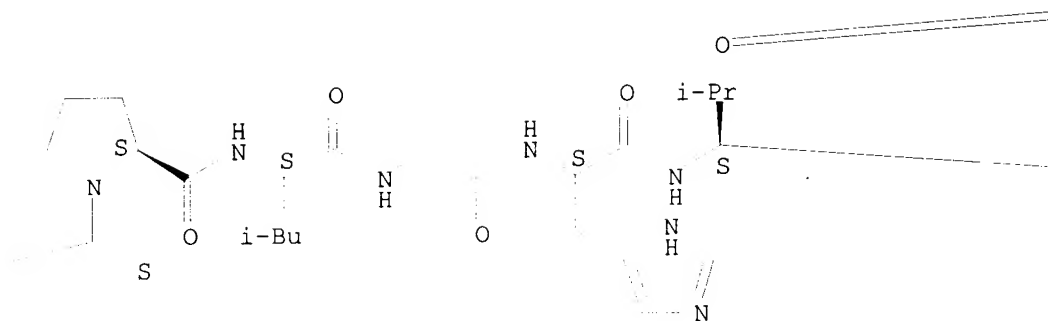
CN L-Valine, 1-[[[4-[[[2-carboxy-1-[3-[[[3-
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 INDEX NAME)

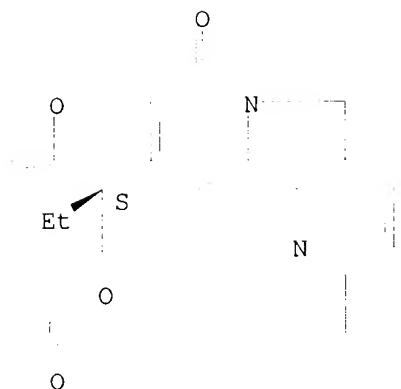
Absolute stereochemistry.

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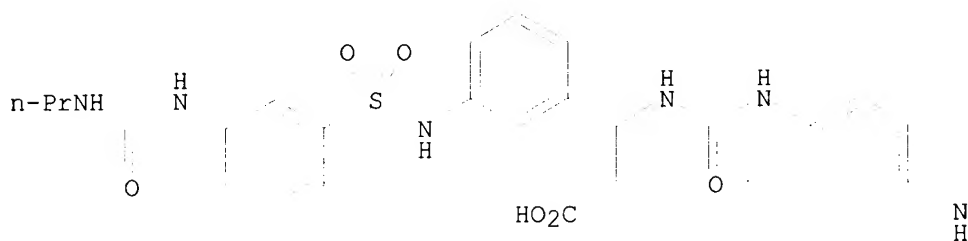
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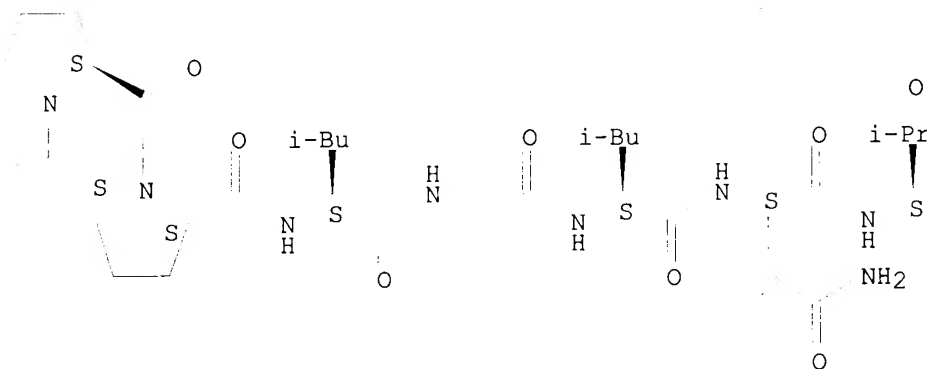


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 leucylglycyl-L-leucyl-L-asparaginyl-, 7-[(4S)-4-ethyl-3,4,12,14-
 tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-
 4-yl] ester (9CI) (CA INDEX NAME)

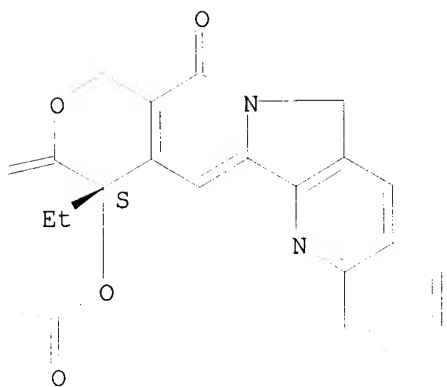
Absolute stereochemistry.



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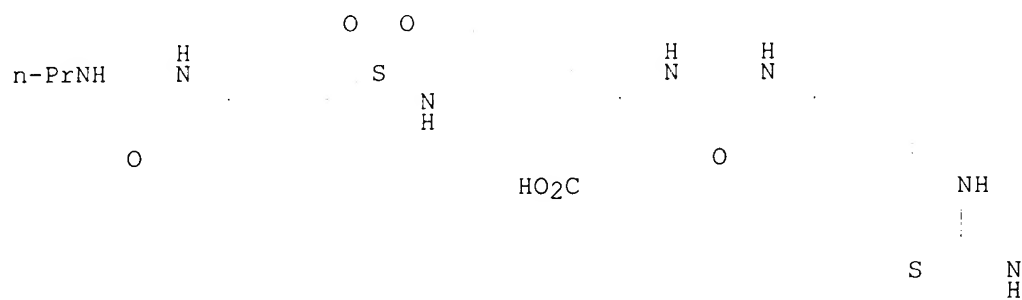
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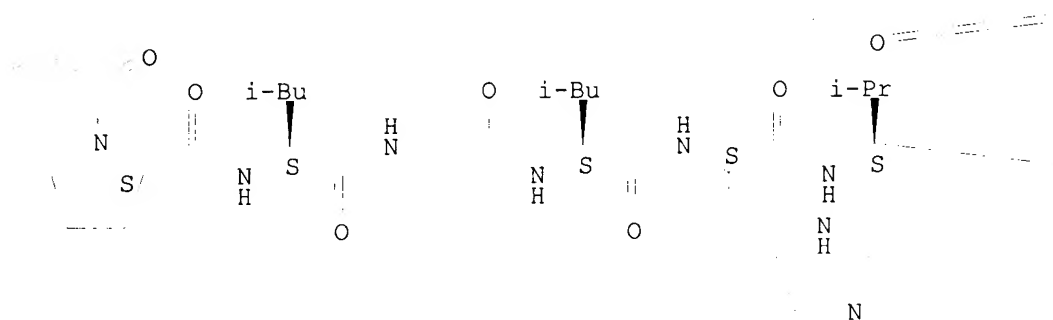
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 leucylglycyl-L-leucyl-L-histidyl-, 7-[(4S)-4-ethyl-3,4,12,14-
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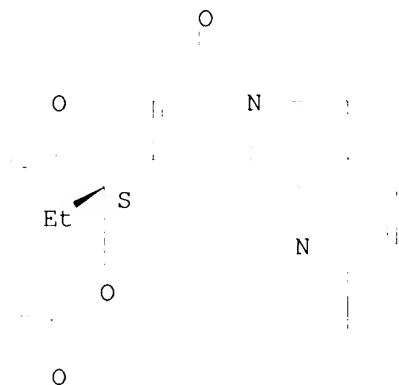
Absolute stereochemistry.

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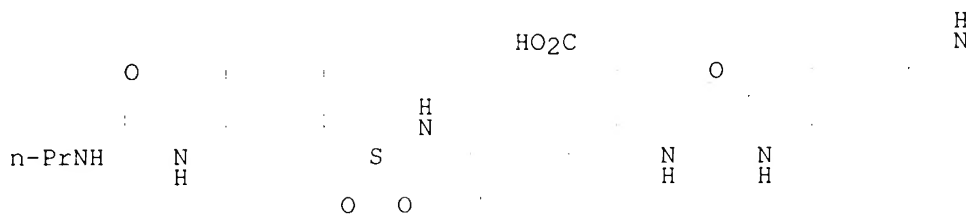
PAGE 1-B

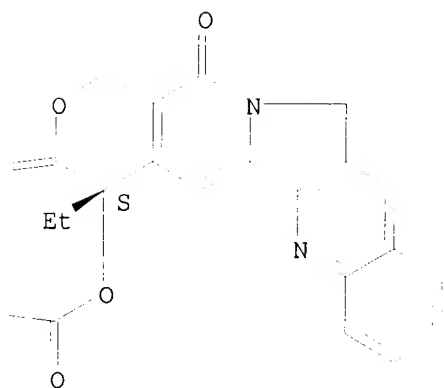
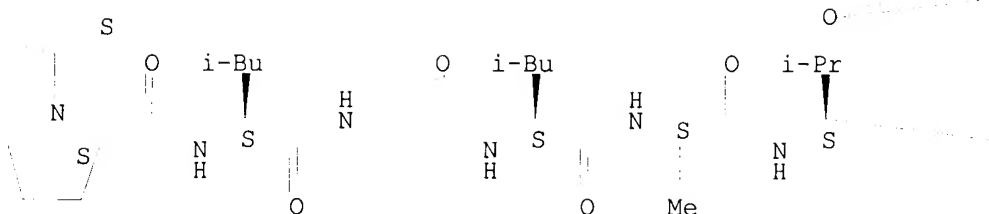




RN 439864-93-4 HCAPLUS
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 L-leucyl-L-alanyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-
 1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester (9CI) (CA
 INDEX NAME)

Absolute stereochemistry.



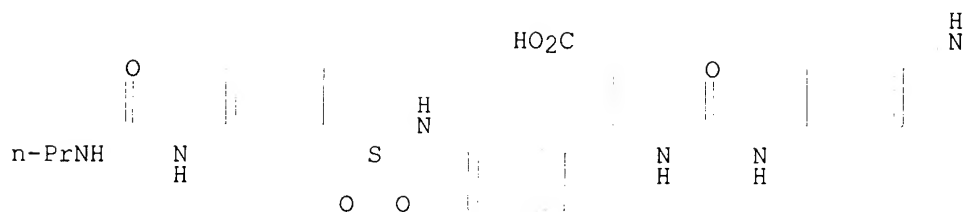


RN 439864-94-5 HCAPLUS

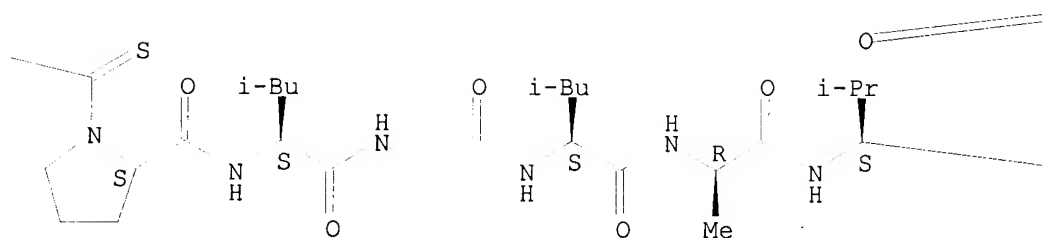
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 L-leucyl-D-alanyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-
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 INDEX NAME)

Absolute stereochemistry.

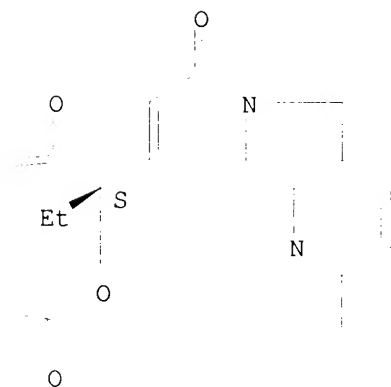
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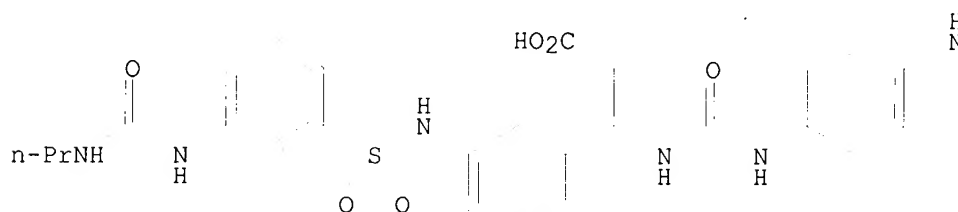
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RN 439864-95-6 HCAPLUS

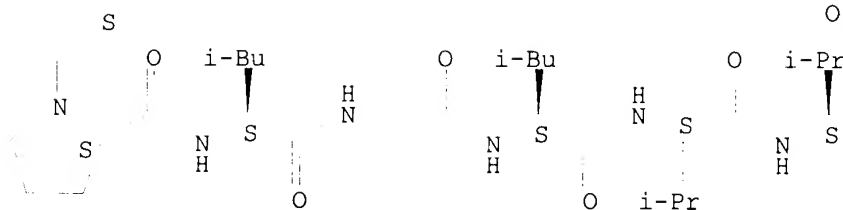
CN L-Valine, 1-[[[4-[[[2-carboxy-1-[3-[[[3-
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no] carbonyl] amino] phenyl] amino] thioxomethyl]-L-prolyl-L-leucylglycyl-
L-leucyl-L-valyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-
1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester (9CI) (CA
INDEX NAME)

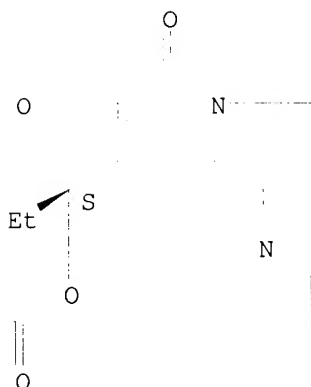
Absolute stereochemistry.

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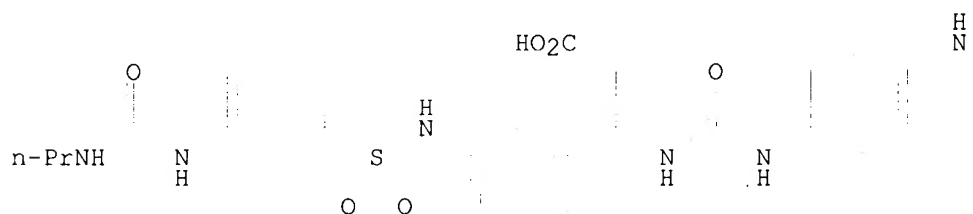




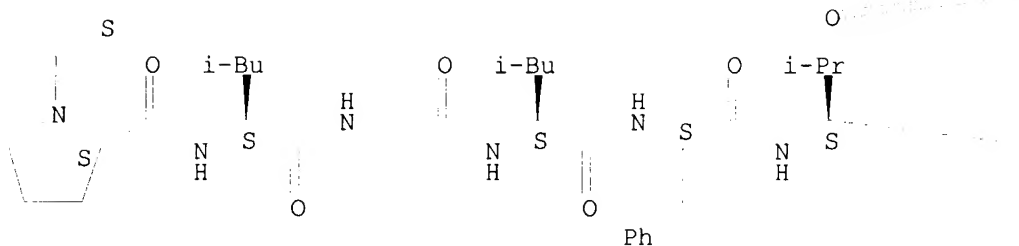
RN 439864-96-7 HCAPLUS

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 L-leucyl-L-phenylalanyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-
 dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester
 (9CI) (CA INDEX NAME)

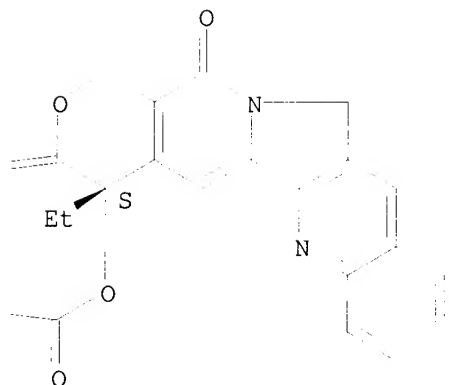
Absolute stereochemistry.



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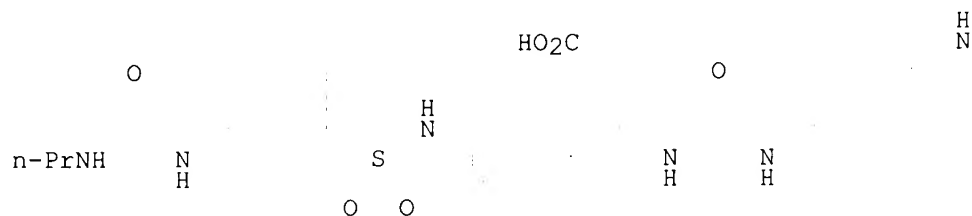


RN 439864-97-8 HCAPLUS

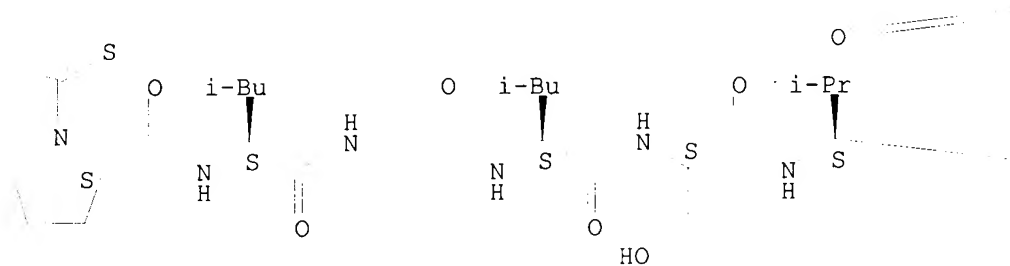
CN L-Valine, 1-[[[4-[[[2-carboxy-1-[3-[[[3-
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 L-leucyl-L-seryl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-
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 INDEX NAME)

Absolute stereochemistry.

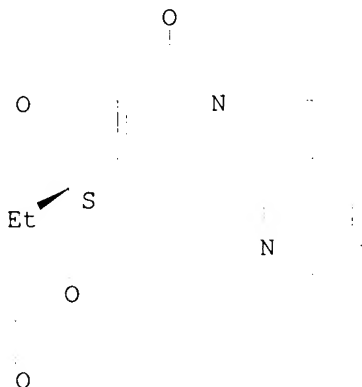
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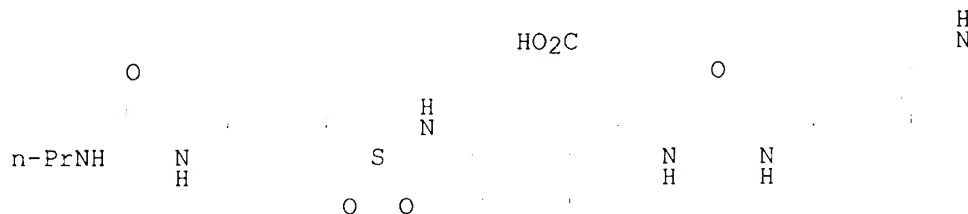


RN 439864-98-9 HCAPLUS

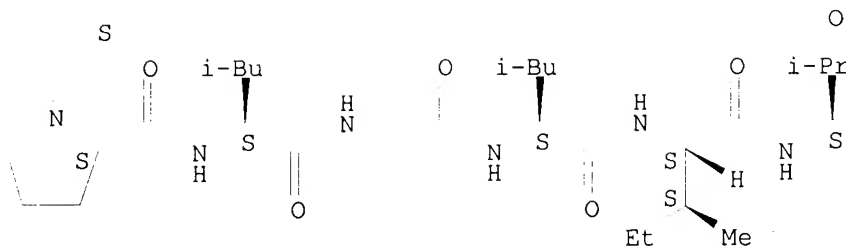
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no] carbonyl] amino] phenyl] amino] thioxomethyl]-L-prolyl-L-leucylglycyl-
L-leucyl-L-isoleucyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-
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(9CI) (CA INDEX NAME)

Absolute stereochemistry.

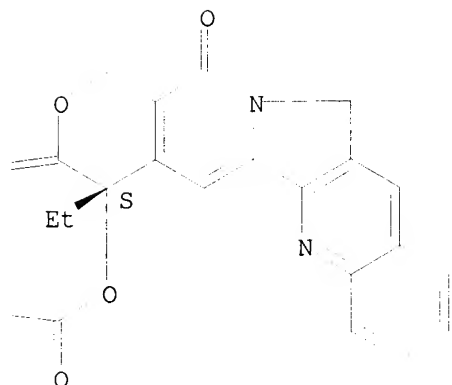
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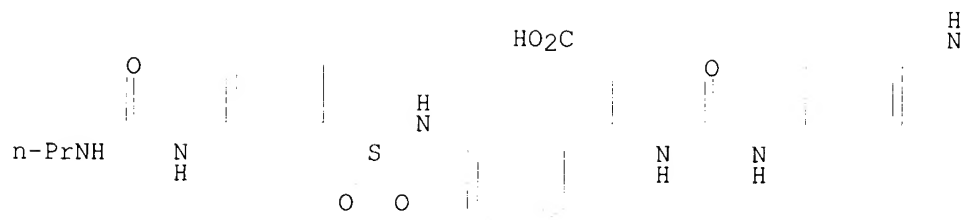


RN 439864-99-0 HCAPLUS

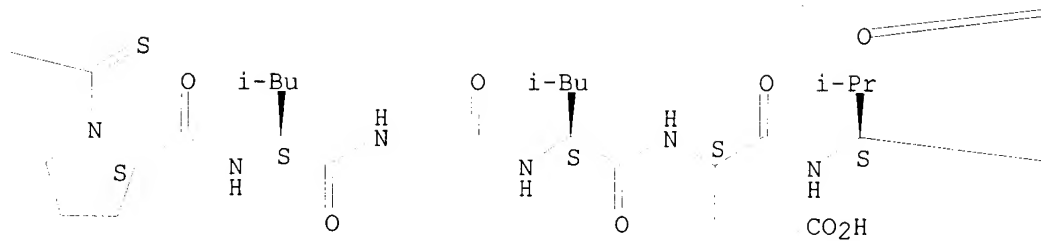
CN L-Valine, 1-[[[4-[[[2-carboxy-1-[3-[[[3-
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 no]carbonyl]amino]phenyl]amino]thioxomethyl]-L-prolyl-L-leucylglycyl-
 L-leucyl-L-.alpha.-glutamyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-
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 (9CI) (CA INDEX NAME)

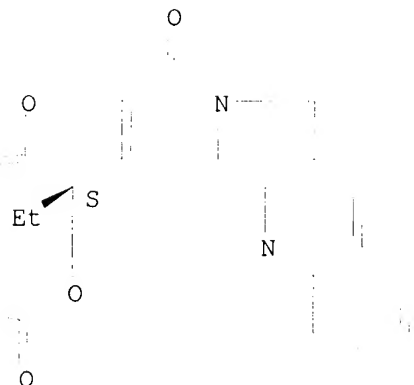
Absolute stereochemistry.

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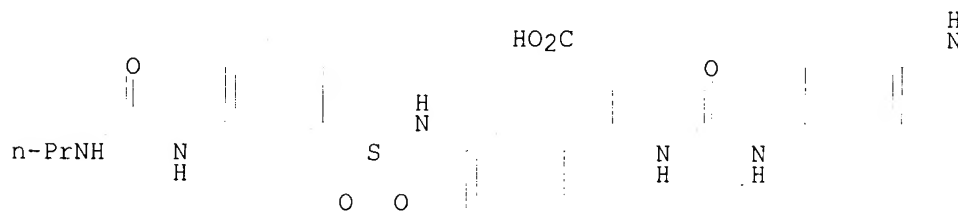


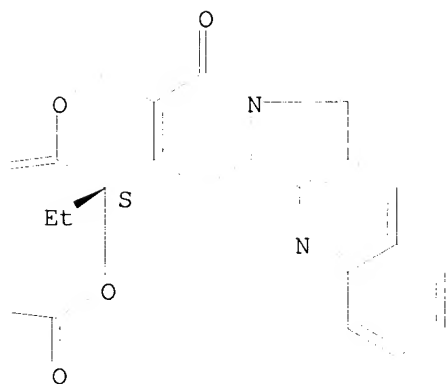
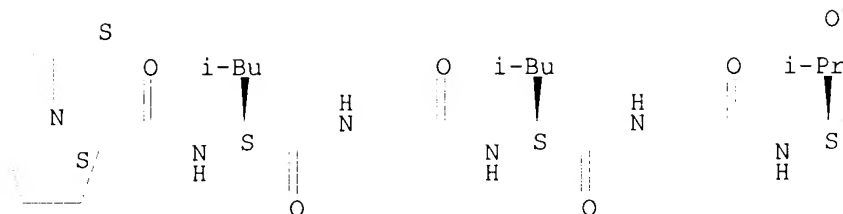


RN 439865-00-6 HCAPLUS

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 L-leucylglycyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-
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 INDEX NAME)

Absolute stereochemistry.



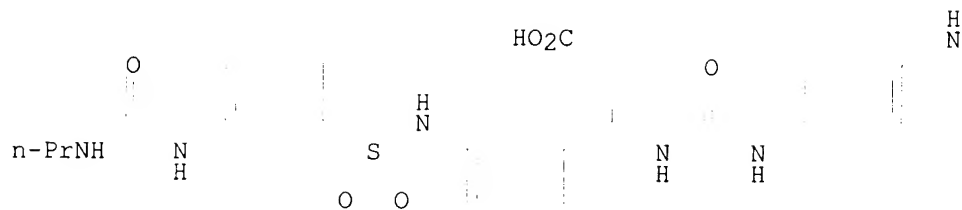


RN 439865-01-7 HCAPLUS

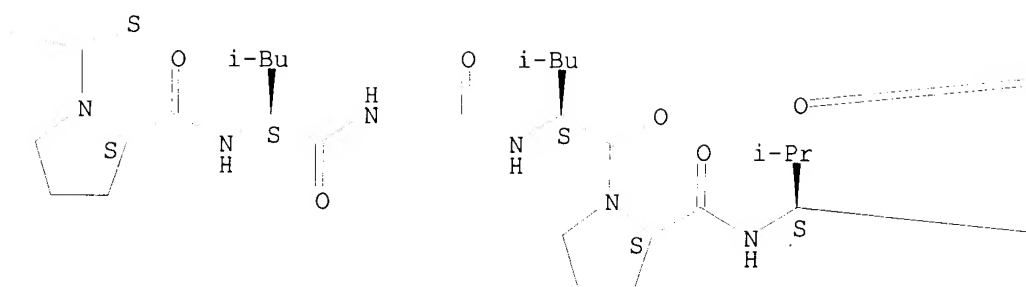
CN L-Valine, 1-[[[4-[[[2-carboxy-1-[3-[[[3-
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 L-leucyl-L-prolyl-, 6-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-
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 INDEX NAME)

Absolute stereochemistry.

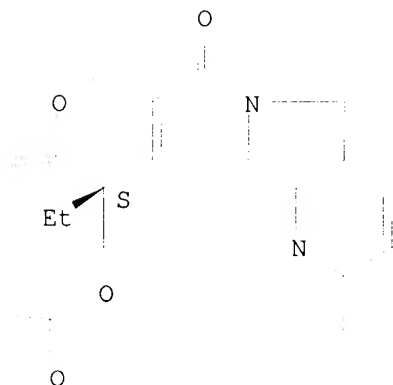
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IT 330155-52-7P 439865-61-9P 439865-65-3P
439865-66-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

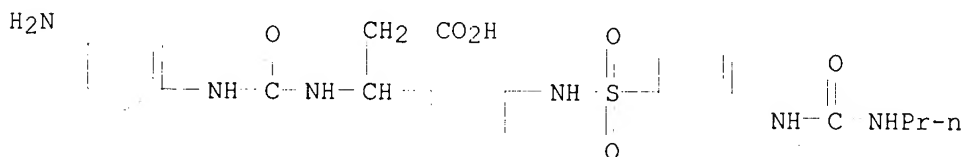
Searcher : Shears 308-4994

RACT (Reactant or reagent)

(prepn. of conjugates of integrin receptor antagonists and a
cytostatic agent having specifically cleavable linking units)

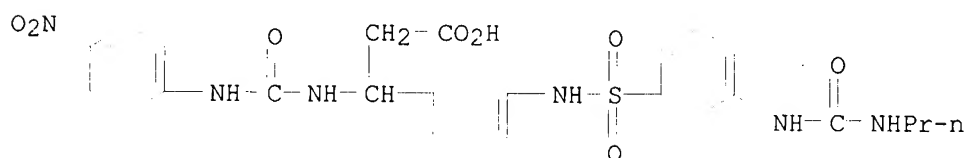
RN 330155-52-7 HCAPLUS

CN Benzenepropanoic acid, .beta.-[[[(4-aminophenyl)amino]carbonyl]amino
]-3-[[[3-[[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]- (9CI)
(CA INDEX NAME)



RN 439865-61-9 HCAPLUS

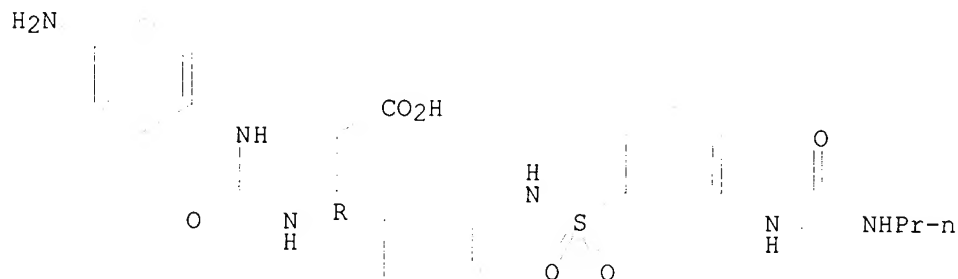
CN Benzenepropanoic acid, .beta.-[[[(4-nitrophenyl)amino]carbonyl]amino
]-3-[[[3-[[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]- (9CI)
(CA INDEX NAME)



RN 439865-65-3 HCAPLUS

CN Benzenepropanoic acid, .beta.-[[[(4-aminophenyl)amino]carbonyl]amino
]-3-[[[3-[[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]-,
(.beta.R)- (9CI) (CA INDEX NAME)

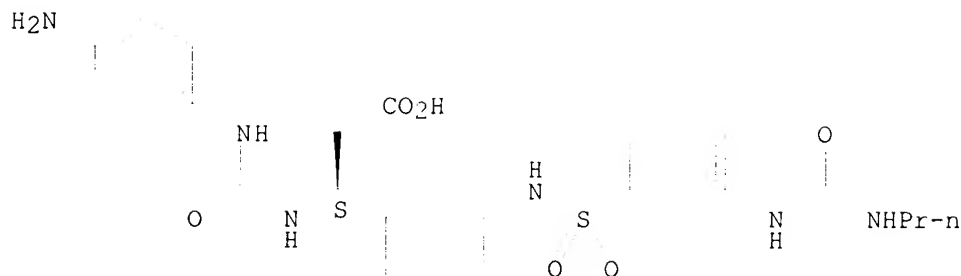
Absolute stereochemistry.



RN 439865-66-4 HCAPLUS

CN Benzenepropanoic acid, .beta.-[[[(4-aminophenyl)amino]carbonyl]amino
]-3-[[[3-[[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]-,
(.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



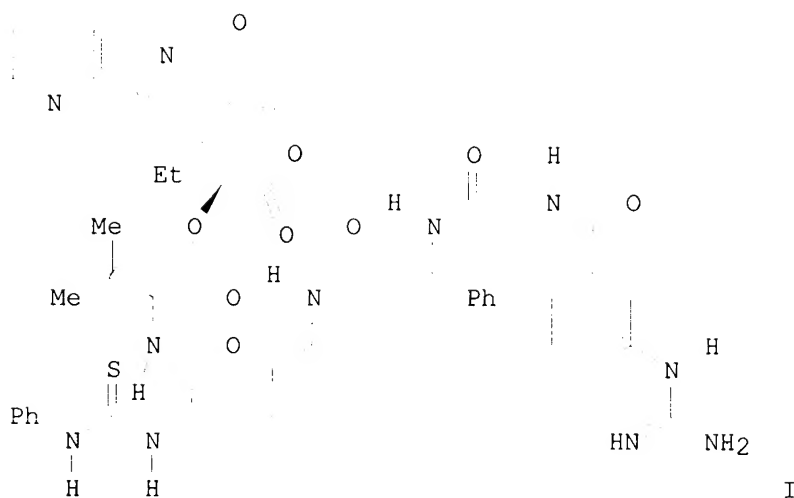
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE
IN THE RE FORMAT

L4 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:185604 HCAPLUS
DOCUMENT NUMBER: 134:237346
TITLE: Preparation of peptidyl camptothecin conjugates
as antitumor agents
INVENTOR(S): Lerchen, Hans-Georg; Baumgarten, Joerg;
Brueggemeier, Ulf; Albers, Markus; Schoop,
Andreas; Schulze, Thomas
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 239 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001017563	A2	20010315	WO 2000-EP8361	20000828
WO 2001017563	A3	20020711		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013883	A	20020507	BR 2000-13883	20000828
EP 1235595	A2	20020904	EP 2000-965901	20000828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-392167 A 19990908
US 2000-606772 A 20000629
WO 2000-EP8361 W 20000828

OTHER SOURCE(S): MARPAT 134:237346
GI



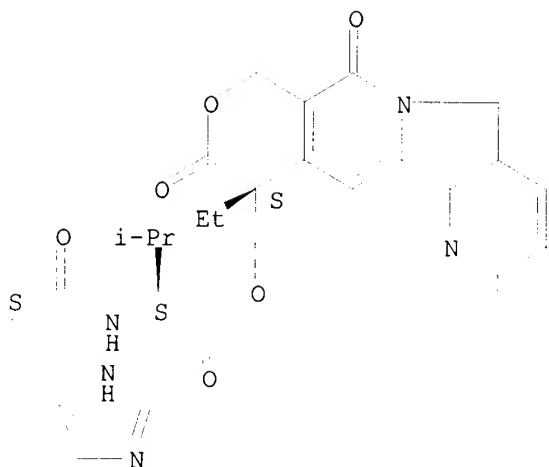
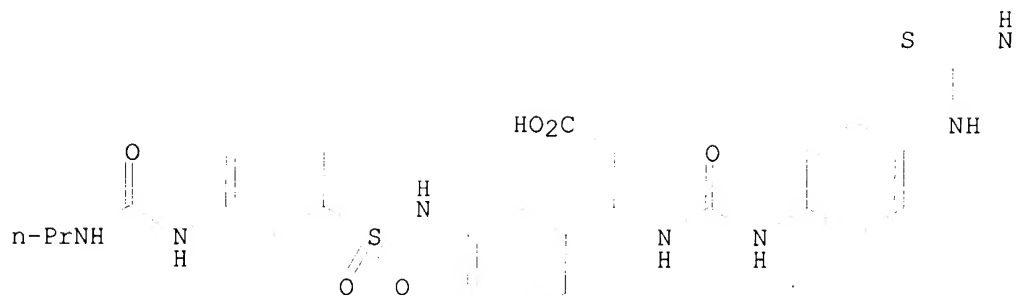
AB Title compds., e.g., I, cytostatics which have a tumor-specific action as a result of linkage to .alpha.V.beta.3 integrin ligands, were prepd.. Data for biol. activity of title compds. were given.

IT **330155-15-2P**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of peptidyl camptothecin conjugates as antitumor agents)

RN 330155-15-2 HCAPLUS

CN L-Valine, N-[[[4-[[[2-carboxy-1-[3-[[[3-[[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]phenyl]ethyl]amino]carbonyl]amino]phenyl]amino]thioxomethyl]-L-histidyl-, 2-[(4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 330155-52-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)

(prepn. of peptidyl camptothecin conjugates as antitumor agents)

RN 330155-52-7 HCAPLUS

CN Benzenepropanoic acid, .beta.-[[[(4-aminophenyl)amino]carbonyl]amino]-3-[[[3-[[(propylamino)carbonyl]amino]phenyl]sulfonyl]amino]- (9CI)
 (CA INDEX NAME)

$$\begin{array}{ccccccc} \text{H}_2\text{N} & & \text{O} & \text{CH}_2 & \text{CO}_2\text{H} & & \text{O} \\ & & | & | & & & | \\ \text{--- NH ---} & \text{C ---} & \text{NH ---} & \text{CH ---} & \text{--- NH ---} & \text{S ---} & \\ & & & & & & | \\ & & & & & & \text{O} \\ & & & & & & | \\ & & & & & & \text{NH --- C --- NHPr-n} \\ & & & & & & | \\ & & & & & & \text{O} \end{array}$$

L6 FILE 'USPATFULL' ENTERED AT 12:51:23 ON 14 FEB 2003
2 S L3

ACCESSION NUMBER: 2002:337946 USPATFULL
TITLE: Novel cytostatic conjugates with integrin ligands
INVENTOR(S): Lerchen, Hans-Georg, Leverkusen, GERMANY, FEDERAL
REPUBLIC OF
Baumgarten, Jorg, Wuppertal, GERMANY, FEDERAL
REPUBLIC OF
Schoop, Andreas, Mittelbiberach, GERMANY, FEDERAL
REPUBLIC OF
Albers, Markus, Leverkusen, GERMANY, FEDERAL
REPUBLIC OF

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2001-105350	20010308
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Jeffrey M. Greenman, Vice President, Patents and Licensing, Bayer Corporation, 400 Morgan Lane, West Haven, CT, 06516	
NUMBER OF CLAIMS:	16	
EXEMPLARY CLAIM:	1	
LINE COUNT:	2658	

AB The present invention relates to cytostatics which have a tumour-specific action as a result of linkage to .alpha..sub.v.beta..sub.3 integrin antagonists via preferred linking units which can be selectively cleaved by elastase, i.e. by an enzyme which can especially be found in tumour tissue. The preferred linking units provide sufficient stability of the conjugate of cytostatic and .alpha..sub.v.beta..sub.3 integrin antagonist in biological fluids and, at the same time, the desired intracellular action within tumour cells as a result of its specific enzymatic or hydrolytic cleavability with release of the cytostatic.

L6 ANSWER 2 OF 2 USPATFULL
ACCESSION NUMBER: 2002:323090 USPATFULL

Searcher : Shears 308-4994

10/026408

TITLE: Cytostatic-integrin conjugates having
specifically cleavable linking units
INVENTOR(S): Lerchen, Hans-Georg, Leverkusen, GERMANY, FEDERAL
REPUBLIC OF
Baumgarten, Jorg, Wuppertal, GERMANY, FEDERAL
REPUBLIC OF
Lockhoff, Oswald, Leverkusen, GERMANY, FEDERAL
REPUBLIC OF
Albers, Markus, Leverkusen, GERMANY, FEDERAL
REPUBLIC OF
Schoop, Andreas, Mittelbiberach, GERMANY, FEDERAL
REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002183256	A1	20021205
APPLICATION INFO.:	US 2001-26408	A1	20011221 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	EP 2000-128401	20001227
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Jeffrey M. Greenman, Vice President, Patents and Licensing, Bayer Corporation, 400 Morgan Lane, West Haven, CT, 06516	
NUMBER OF CLAIMS:	21	
EXEMPLARY CLAIM:	1	
LINE COUNT:	5098	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to cytostatics which have a tumor-specific action as a result of linkage to .alpha..sub.v.beta..sub.3 integrin antagonists via preferred linking units which can be selectively cleaved by enzymes such as metallo matrixproteases (MMPs), i.e. by enzymes which can especially be found in tumor tissue. The preferred linking units guarantee the serum stability of the conjugate of cytostatic and .alpha..sub.v.beta..sub.3 integrin antagonist and, at the same time, the desired intracellular action within tumor cells as a result of its specific enzymatic or hydrolytic cleavability with release of the cytostatic.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MARPAT' ENTERED AT 12:51:41 ON 14 FEB 2003)
L1 STR

10/026408

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          18
      NH 12

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  17   16           O

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NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

GGCAT IS UNS AT 2

GGCAT IS UNS AT 5

GGCAT IS UNS AT 15

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

MLEVEL IS CLASS ON RING NODES AND RING GROUPS

MLEVEL IS CLASS ON CHAIN NODES AND CHAIN GROUPS

ECLEVEL IS LIM ON ALL NODES

ALL RING(S) ARE ISOLATED

L8 5 SEA FILE=MARPAT SSS FUL L1 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 14824 ITERATIONS (2 INCOMPLETE) 5 ANSWERS
SEARCH TIME: 00.01.12

L8 ANSWER 1 OF 5 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 137:210930 MARPAT

TITLE: Enzyme-activated cytostatic conjugates with
integrin ligands

INVENTOR(S): Lerchen, Hans-georg; Baumgarten, Joerg; Schoop,
Andreas; Albers, Markus

PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany

SOURCE: Eur. Pat. Appl., 72 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Searcher : Shears 308-4994

EP 1238678 A1 20020911 EP 2001-105350 20010308
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
 PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 WO 2002072151 A1 20020919 WO 2002-EP2501 20020307
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
 LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
 NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
 TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
 CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
 SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG
 US 2002193311 A1 20021219 US 2002-96120 20020308
 PRIORITY APPLN. INFO.: EP 2001-105350 20010308
 AB The present invention relates to cytostatics which have a
 tumor-specific action as a result of linkage to .alpha.v.beta.3
 integrin antagonists via preferred linking units which can be
 selectively cleaved by elastase, i.e. by an enzyme which can esp. be
 found in tumor tissue. The preferred linking units provide
 sufficient stability of the conjugate of cytostatic and
 .alpha.v.beta.3 integrin antagonist in biol. fluids and, at the same
 time, the desired intracellular action within tumor cells as a
 result of its specific enzymic or hydrolytic cleavability with
 release of the cytostatic.
 IC ICM A61K047-48
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 25, 28, 34, 63
 ST enzyme activated cytostatic conjugate integrin ligand
 IT Antitumor agents
 (carcinoma; enzyme-activated cytostatic conjugates with integrin
 ligands which can be selectively cleaved by elastase in relation
 to toxicity to hemopoietic stem cells)
 IT Cytotoxic agents
 Human
 Solid phase synthesis
 (enzyme-activated cytostatic conjugates with integrin ligands
 which can be selectively cleaved by elastase in relation to
 toxicity to hemopoietic stem cells)
 IT Toxicity
 (hemotoxicity; enzyme-activated cytostatic conjugates with
 integrin ligands which can be selectively cleaved by elastase in
 relation to toxicity to hemopoietic stem cells)
 IT Carcinoma
 (inhibitors; enzyme-activated cytostatic conjugates with integrin
 ligands which can be selectively cleaved by elastase in relation
 to toxicity to hemopoietic stem cells)
 IT Drug delivery systems
 (prodrugs; enzyme-activated cytostatic conjugates with integrin
 ligands which can be selectively cleaved by elastase in relation
 to toxicity to hemopoietic stem cells)
 IT Hematopoietic precursor cell
 (stem, toxicity to; enzyme-activated cytostatic conjugates with
 integrin ligands which can be selectively cleaved by elastase in
 relation to toxicity to hemopoietic stem cells)
 IT Integrins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (.alpha.v.beta.3; enzyme-activated cytostatic conjugates with
 integrin ligands which can be selectively cleaved by elastase in
 relation to toxicity to hemopoietic stem cells)

IT 455940-45-1P 455940-48-4P 455940-51-9P 455940-53-1P
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
 activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (enzyme-activated cytostatic conjugates with integrin ligands
 which can be selectively cleaved by elastase in relation to
 toxicity to hemopoietic stem cells)

IT 9004-06-2, Elastase
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (enzyme-activated cytostatic conjugates with integrin ligands
 which can be selectively cleaved by elastase in relation to
 toxicity to hemopoietic stem cells)

IT 7689-03-4, 20(S)-Camptothecin
 RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL
 (Biological study); RACT (Reactant or reagent)
 (enzyme-activated cytostatic conjugates with integrin ligands
 which can be selectively cleaved by elastase in relation to
 toxicity to hemopoietic stem cells)

IT 455940-58-6P 455940-60-0P
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN
 (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
 study); PREP (Preparation); USES (Uses)
 (enzyme-activated cytostatic conjugates with integrin ligands
 which can be selectively cleaved by elastase in relation to
 toxicity to hemopoietic stem cells)

IT 455940-55-3P 455940-63-3P 455940-65-5P 455940-67-7P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (enzyme-activated cytostatic conjugates with integrin ligands
 which can be selectively cleaved by elastase in relation to
 toxicity to hemopoietic stem cells)

IT 7689-03-4D, Camptothecin, conjugates
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (enzyme-activated cytostatic conjugates with integrin ligands
 which can be selectively cleaved by elastase in relation to
 toxicity to hemopoietic stem cells)

IT 67-63-0, 2-Propanol, reactions 99-61-6, 3-Nitrobenzaldehyde
 100-28-7, 4-Nitrophenyl isocyanate 107-10-8, Propylamine,
 reactions 110-78-1, Propyl isocyanate 121-51-7,
 3-Nitrobenzenesulfonyl chloride 2937-50-0, Allyloxycarbonyl
 chloride 3392-05-0 3392-12-9 4125-93-3 13139-15-6,
 N-(tert-Butoxycarbonyl)leucine 205687-19-0 282525-10-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (enzyme-activated cytostatic conjugates with integrin ligands
 which can be selectively cleaved by elastase in relation to
 toxicity to hemopoietic stem cells)

IT 283613-06-9P 283613-07-0P 330155-29-8P 330155-52-7P
 330155-53-8P 455940-71-3P 455940-75-7P 455940-80-4P
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 455940-98-4P 455941-04-5P 455941-07-8P 455941-11-4P
 455941-15-8P 455941-17-0P 455941-19-2P 455941-21-6P

10/026408

455941-23-8P 455941-25-0P 455941-26-1P 455941-27-2P
455941-28-3P 455941-29-4P 455941-30-7P 455941-31-8P
455941-32-9P 455941-33-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)

(enzyme-activated cytostatic conjugates with integrin ligands
which can be selectively cleaved by elastase in relation to
toxicity to hemopoietic stem cells)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN
THE RE FORMAT

L8 ANSWER 2 OF 5 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 134:237346 MARPAT

TITLE: Preparation of peptidyl camptothecin conjugates
as antitumor agents

INVENTOR(S): Lerchen, Hans-Georg; Baumgarten, Joerg;
Brueggemeier, Ulf; Albers, Markus; Schoop,
Andreas; Schulze, Thomas

PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Germany

SOURCE: PCT Int. Appl., 239 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

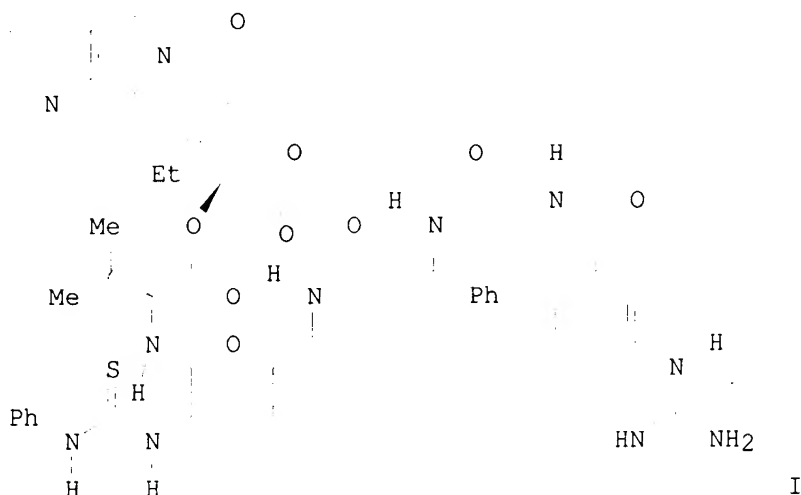
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001017563	A2	20010315	WO 2000-EP8361	20000828
WO 2001017563	A3	20020711		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
BR 2000013883	A	20020507	BR 2000-13883	20000828
EP 1235595	A2	20020904	EP 2000-965901	20000828
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
PRIORITY APPLN. INFO.:			US 1999-392167	19990908
			US 2000-606772	20000629
			WO 2000-EP8361	20000828

GI



- AB Title compds., e.g., I, cytostatics which have a tumor-specific action as a result of linkage to .alpha.V.beta.3 integrin ligands, were prepd.. Data for biol. activity of title compds. were given.
- IC ICM A61K047-48
- CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 34
- ST peptidyl camptothecin conjugate prepn antitumor agent
- IT Antitumor agents
(peptidyl camptothecin conjugates)
- IT Integrins
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(.alpha.v.beta.3; prepn. of peptidyl camptothecin conjugates as antitumor agents)
- IT Integrins
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(.alpha.v.beta.5; prepn. of peptidyl camptothecin conjugates as antitumor agents)
- IT
- | | | | |
|--------------|--------------|--------------|--------------|
| 330154-85-3P | 330154-86-4P | 330154-87-5P | 330154-88-6P |
| 330154-89-7P | 330154-90-0P | 330154-91-1P | 330154-92-2P |
| 330154-93-3P | 330154-94-4P | 330154-95-5P | 330154-96-6P |
| 330154-97-7P | 330154-98-8P | 330154-99-9P | 330155-00-5P |
| 330155-01-6P | 330155-02-7P | 330155-03-8P | 330155-04-9P |
| 330155-06-1P | 330155-08-3P | 330155-09-4P | 330155-10-7P |
| 330155-11-8P | 330155-12-9P | 330155-13-0P | 330155-14-1P |
| 330155-15-2P | 330155-16-3P | 330155-17-4P | 330155-18-5P |
| 330155-20-9P | 330155-22-1P | 330155-24-3P | 330155-25-4P |
| 330155-26-5P | 330155-27-6P | 330155-28-7P | |
- RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptidyl camptothecin conjugates as antitumor agents)
- IT 98-09-9, Benzenesulfonyl chloride 98-58-8, 4-Bromobenzenesulfonyl chloride 98-74-8, p-Nitrobenzenesulfonyl chloride 99-61-6,

3-Nitrobenzaldehyde 100-28-7, 4-Nitrophenyl isocyanate 100-52-7,
 Benzaldehyde, reactions 103-72-0, Phenyl isothiocyanate
 107-10-8, Propylamine, reactions 108-30-5, Succinic anhydride,
 reactions 121-51-7, 3-Nitrobenzenesulfonyl chloride 121-90-4,
 3-Nitrobenzoyl chloride 141-82-2, Malonic acid, reactions
 150-13-0, p-Aminobenzoic acid 934-32-7, 2-Aminobenzimidazole
 2905-24-0, 3-Bromobenzenesulfonyl chloride 2937-50-0, Allyl
 chloroformate 3392-07-2 7689-03-4, (S)-Camptothecin 13030-09-6
 13331-27-6, 3-Nitrophenylboronic acid 21286-54-4,
 (1S)-10-Camphorsulfonyl chloride 23095-05-8, 5-Bromo-2-
 methoxybenzenesulfonyl chloride 30418-59-8, 3-Aminophenylboronic
 acid 91421-43-1, 9-Aminocamptothecin 95753-55-2 141468-55-5
 180181-93-5 269078-76-4

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of peptidyl camptothecin conjugates as antitumor agents)

IT 150-30-1P, Phenylalanine 6335-76-8P, Ethyl 3-amino-3-
 phenylpropionate 188803-59-0P 188803-62-5P 188805-48-3P
 188812-76-2P 188815-24-9P 205687-80-5P 205687-87-2P
 205688-17-1P 276260-09-4P 276260-12-9P 276260-17-4P
 282525-10-4P 283613-06-9P 283613-07-0P 283613-08-1P
 283613-09-2P 283613-10-5P 283613-11-6P 283613-55-8P
 283613-56-9P 283613-57-0P 283613-58-1P 283613-59-2P
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 330155-63-0P 330155-64-1P 330155-65-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)

(prepn. of peptidyl camptothecin conjugates as antitumor agents)

L8 ANSWER 3 OF 5 MARPAT COPYRIGHT 2003 ACS

ACCESSION NUMBER: 133:105343 MARPAT

TITLE: Preparation of .beta.-phenylalanine derivatives
 as integrin antagonists

INVENTOR(S): Schoop, Andreas; Muller, Gerhard; Bruggemeier,
 Ulf; Schmidt, Delf; Stelte-Ludwig, Beatrix;
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PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: PCT Int. Appl., 129 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

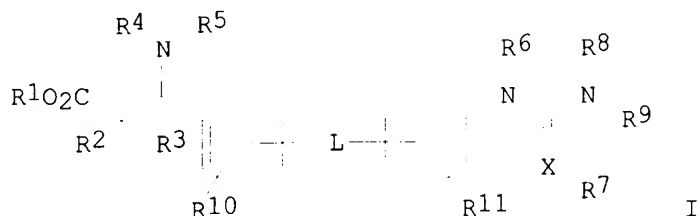
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041469	A2	20000720	WO 2000-EP120	20000111
WO 2000041469	A3	20001116		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
 CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
 ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,

10/026408

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6291503 B1 20010918 US 1999-232738 19990115
CA 2360356 AA 20000720 CA 2000-2360356 20000111
EP 1147079 A2 20011024 EP 2000-903571 20000111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
PT, IE, SI, LT, LV, FI, RO
JP 2002534439 T2 20021015 JP 2000-593094 20000111
US 2001031788 A1 20011018 US 2001-867835 20010530
PRIORITY APPLN. INFO.: US 1999-232738 19990115
WO 2000-EP120 20000111

GI



AB .beta.-Phenylalanine derivs. I [R1 = H, (un)substituted alkyl, cycloalkyl, aryl, heterocyclyl; R2, R3 = any group given for R1 or (un)substituted alkenyl or alkynyl, OH, alkoxy or R2 and R3 are bonded to each other; R4 = carboxy ester, SO2H, CHO, CONH2, C(S)NH2 or their derivs.; R5 = H, (un)substituted alkyl, cycloalkyl, aryl; R6 = any group given for R1 or is bonded to one of R7, R8 or R9; R7 is absent, H, (un)substituted alkyl or cycloalkyl, NO2, CN, CHO or CO2H or their derivs., or is bonded to one of R6, R8, or R9; R8, R9 = any group given for R1 or is bonded to one of R6, R7 or R9 or R8; R10, R11 = H, (un)substituted alkyl, cycloalkyl, or alkoxy, halo; L is a sulfonamide, amide, ether, ester, keto, urea, thioether, sulfoxide or sulfone unit optionally extended by one or two methylene groups; X is N, O or S] and their physiol. acceptable salts and stereoisomers were prepd. Thus, 3-[(phenylsulfonyl)amino]-3-[3-[(3-guanidinophenyl)sulfonyl]phenyl]propionic acid trifluoroacetic acid salt, prepd. by a multistep procedure from 3-nitrobenzaldehyde, ammonium acetate, malonic acid, benzenesulfonyl chloride, 3-nitrobenzenesulfonyl chloride, and 1,3-bis(tert-butoxycarbonyl)-2-methyl-2-thiopseudourea, showed IC50 = 19 nM antagonist activity against integrin .alpha.v.beta.3 receptor.

IC C07D401-00

CC 34-2 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

ST phenylalanine beta deriv prepn integrin antagonist

IT Angiogenesis

Antitumor agents

Arteriosclerosis

Eye, disease

Osteoporosis

Rheumatoid arthritis